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The American Heart Journal

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The American Heart Journal

VOL. 11 FEBRUARY, 1936 NO. 2

Original Communications

DIASTOLIC GALLOP RHYTHM

A NOTE ON CERTAIN FACTORS INFLUENCING PROGNOSIS*†

WILLIAM PAUL THOMPSON, M.D., AND SAMUEL A. LEVINE, M.D.
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THE grave prognostic significance of diastolic gallop rhythm of the heart sounds is well known. A study of 89 cases, however, has shown some differences in prognosis according to simple findings easily made at the bedside. We propose to present such factors as may be of some aid in predicting the prognosis of the individual patient and shall not attempt to include all such factors or those which have been adequately emphasized previously.

All of the patients in this series were seen in the private practice of one of us during the past twelve years. Auscultation was the only means used for the detection of the gallop sound. We have made no attempt to separate protodiastolic, mesodiastolic, and presystolic gallop rhythm for the purposes of this study because of the uncertainty entailed in the proper classification of these forms clinically. We are given support for this apparent neglect in the recent work of Wolferth and Margolies,[1] who have shown by electrophonocardiographic studies that gallop sounds protodiastolic in origin may actually be closer to the normal first sound than to the second and that sounds presystolic in origin may be closer to the second sound. This apparent displacement of the extra sound is, of course, a function of cardiac rate. Since diastolic gallop rhythm occurs relatively infrequently at slow rates, we believe the clinical classification of the various forms to be usually impracticable if not often wholly erroneous.

Only patients who were known to be dead and the duration of whose lives after the detection of gallop rhythm was known to us were selected. There was a total of 192 patients in whom diastolic gallop

*From the Medical Clinic of the Peter Bent Brigham Hospital.

†Aided by a grant from the Proctor Fund of Harvard University for the Study of Chronic Diseases.

rhythm was observed during the twelve years. Ninety, or 47 per cent, are known to be dead. The duration of life was known to us in 89 cases. The average life for these was ten months and twenty days. The remainder were either still alive, or follow-up data regarding them were not available. A review of the present clinical condition of those we know to be still living led us to believe that the figures we shall present would have been somewhat altered if the entire group had been followed until death. A lengthening of the duration of life after the detection of gallop rhythm would probably result because of the inclusion of a few patients who had no organic heart disease (a normal third heart sound resembling gallop rhythm) and some patients with acute rheumatic carditis with delayed auriculoventricular conduction time who often have a satisfactory prognosis.

General Considerations.—All of the eighty-nine patients had organic cardiovascular disease. Seventy-six per cent were males; 24 per cent were females. There were only seven patients under forty years of age and only eight seventy years old or older. The youngest was ten years old; the oldest was seventy-five. Coronary artery disease was predominant etiologically, making up 52 per cent of the series. About two-thirds of these had coronary occlusions. Thirty-eight per cent

TABLE I

	NUMBER OF CASES	AVERAGE DURATION OF LIFE		
		YEARS	MONTHS	DAYS
Total cases	89	0	10	20
Hypertensive cardiovascular disease	34	0	11	22
Coronary artery disease (including angina pectoris)	46	0	10	15
Without coronary occlusion	16	1	3	17
With coronary occlusion	30	0	7	24
Gallop appearing during acute infarction	14	0	4	29
Rheumatic heart disease	6	0	1	28
Etiology unknown	3	1	0	15
Age: Below 40 years	7	0	2	24
40 to 49 years	17	0	8	14
50 to 59 years	30	0	10	29
60 to 69 years	27	0	9	25
70 years and over	8	1	11	25
Sex: Males	68	0	10	19
Females	21	0	10	21
Total with hypertension	63	1	0	15
Total without hypertension	23	0	6	3
Systolic blood pressure: Below 120 mm.	10	0	0	22
120 to 149 mm.	18	0	9	7
150 to 199 mm.	34	1	1	25
200 mm. and above	24	0	11	27
Diastolic blood pressure: Below 90 mm.	20	0	5	11
90 to 99 mm.	13	1	8	0
100 to 119 mm.	27	1	0	16
120 mm. and above	26	0	8	23
Frank congestive failure	38	0	6	17
Without congestive failure	51	1	0	14
Intraventricular heart-block	16	1	5	8
Normal intraventricular conduction	30	0	11	23

had hypertensive cardiovascular disease. Arterial hypertension was common in the other etiological groups, so that a total of 71 per cent of the entire series had abnormally elevated blood pressures. Only six patients had rheumatic heart disease, none of whom had mitral stenosis. These divisions accounted for all but three patients the etiology of whose disease is unknown. The heart was clinically enlarged in 87 per cent. Forty-three per cent had frank congestive failure at the time gallop rhythm was first detected. A number of the

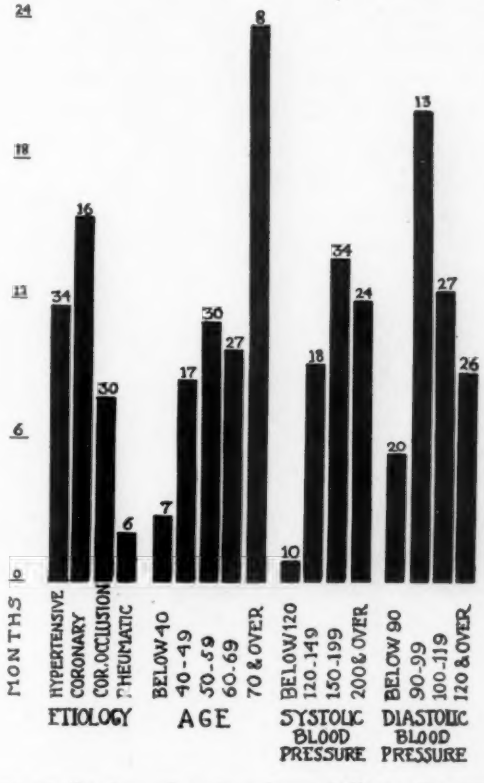

Fig. 1.—The figures at the top of each column indicate the number of patients represented.

others developed failure later. Symptoms of myocardial insufficiency were marked in the group as a whole. Normal sinus rhythm was present in every instance.

Relation of Etiology to Prognosis.—There was little difference in the length of life after detection of diastolic gallop according to the etiological diagnosis, except in the group with rheumatic heart disease. These lived an average of only about two months, a very much shorter time than either of the other two groups. This group is too small, however, to have the figures conclusive. These and the other data are shown in Table I and Fig. 1.

Coronary Occlusion.—The patients with coronary artery disease who had never suffered an occlusion at the time diastolic gallop was first detected lived about twice as long as those who had suffered an occlusion at some time, either in the past or recently. If the gallop appeared during the course of an acute myocardial infarction, the average length of life was very short. The figures in this particular, as given in the table, do not tell all the facts, however. There were fourteen patients whose gallop sounds appeared during acute infarction. Only three of these lived longer than six weeks. One lived three months. One was a physician whose gallop appeared the day following a coronary occlusion. It had disappeared by the next day and was not heard again. He made an excellent recovery and returned to active practice. More than four years later the gallop rhythm was heard again, and in another month he was dead. The third patient in this group lived twenty-one months, but since he was seen only once, it is not known whether the gallop disappeared. Another patient not included in this series had an occlusion over four years before, during the course of which gallop appeared. It disappeared, he made a good recovery, and he is still living and in good health. It would seem, then, that when gallop rhythm appears during the course of an acute myocardial infarction, the prognosis is exceedingly poor but that disappearance of the gallop is a favorable sign.

Age.—The patients who were under forty years of age at the time gallop rhythm was discovered lived on the average only about three months. Those who were seventy years or more of age averaged about two years of life. Between these extremes, i.e., between forty and seventy years, there was no significant difference in the duration of life or difference from the general average. Because of the fact that most of the patients with gallop rhythm were between forty and seventy years of age, these figures have no particular significance in the majority of patients. They are of importance, however, in the younger patients, in whom the prognosis was particularly bad, and in the older ones, in whom it was particularly good as compared to the general average.

Sex.—The duration of life in the males and in the females in this series was practically identical.

Blood Pressure.—The patients with arterial hypertension lived approximately twice as long as did those without it. Those with low systolic pressures, below 120 mm., lived on the average less than one month. With rising systolic pressure the averages became much better, particularly after a level of 150 mm. was reached. When the patients are grouped according to their diastolic pressures, a more

striking difference is seen. Those with diastolic pressures below 90 mm. lived less than six months, while those with pressures between 90 and 99 mm. lived an average of twenty months. When the diastolic pressure was elevated to figures of 100 mm. or more, the average fell considerably. Elevated systolic tensions and slightly elevated diastolic tensions were then favorable prognostic signs, on comparison with the rest of the series, while a systolic tension of less than 120 mm. was a particularly unfavorable sign. Giroux[2] has intimated that gallop rhythm in the presence of hypotension bears a somber prognosis, particularly in the chronic myocardial diseases.

Congestive Failure.—The patients who were in a state of frank congestive failure at the time gallop rhythm was first detected lived on the average about six and one-half months, while those who had never been in failure lived almost twice as long. This may seem an unreasonable comparison because of the obviously poorer prognosis in the patient whose heart has failed, but the fact remains that the presence of congestive signs increased the gravity of this physical sign. Many of the patients who were grouped as having no failure, of course, did develop failure later, but our attempt was made to predict the future of the individual patient at the time gallop rhythm was first observed. White[3] has also mentioned the grave prognosis when heart failure is responsible for the gallop.

Intraventricular Heart-Block.—The presence of intraventricular block, in most cases typical left bundle-branch block, did not have the unfavorable influence on prognosis which might have been expected. In fact, those with such a conduction defect actually lived about 50 per cent longer than those known not to have it, and over 60 per cent longer than the general average. Defective intraventricular conduction was, then, actually a favorable finding. Eppinger and Levine[4] found the same favorable effect of intraventricular block in a series of patients with angina pectoris.

SUMMARY AND CONCLUSIONS

The average duration of life in eighty-nine patients after the detection of diastolic gallop rhythm was ten months and twenty days. Certain easily detectable bedside findings which appeared to alter this prognosis have been studied.

Although there were but a few patients with rheumatic heart disease, the duration of life in them was markedly shorter than when some other etiology was responsible.

Gallop rhythm occurring during the early hours or days following an acute coronary closure had an extremely bad prognostic significance. Its subsequent disappearance, however, was a favorable sign.

Diastolic gallop in patients under forty years of age had a particularly ominous significance, while in patients of seventy or more years the prognosis was relatively good.

The sex of the patient seemed to have no bearing on the duration of life.

The prognosis was poorer in patients without hypertension than in those with it, particularly if the systolic tension was below 120 mm.

The patients with congestive failure at the time gallop was first found lived about half as long, on the average, as those who had not had failure.

The existence of intraventricular heart-block not only did not make the prognosis worse but actually seemed to make it more favorable.

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PULSUS ALTERNANS

A Note on Certain Factors Influencing Prognosis*†

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SEVERAL factors which have a bearing on the duration of life of patients with alternation of the pulse have come to our attention. It has been abundantly confirmed in an extensive literature that pulsus alternans is an ominous sign and that the patient with it will generally not live more than a few years. This was well demonstrated some time ago by Mackenzie[1] and by Windle.[2] We have noticed several factors, easily detectable at the bedside, which influenced the duration of life in our cases and which may allow us somewhat greater accuracy in predicting the outcome for the individual patient. We shall make no attempt to discuss all the factors concerned. We wish only to present some which have not been mentioned or have been inadequately emphasized in the literature.

All of the patients reported here were seen in the private practice of one of us. The alternation was detected by means of the sphygmomanometer, and all cases were constant in type, as contrasted to alternation which occurs for but a few cycles following premature contractions. There were no cases of pseudo-alternation due to bigeminy.

One hundred seventeen patients with alternation have been observed during the past twelve years. This study will be confined to the seventy-one who are known to be dead and the dates of whose deaths are known to us. The others are either still alive or the eventual outcome is unknown. A study of their records led us to believe that the figures to be presented would not have been materially changed if the entire series of 117 had been followed to death. It is obvious that pulsus alternans of the type that occurs only during a paroxysm of tachycardia is not included in this study. One such patient who had typical alternation observed in 1914, when the heart rate was 250, is alive and well today without any cardiac disability.

General Aspects of the Group.—All of the seventy-one patients had organic cardiovascular disease. Hypertensive cardiovascular disease and coronary artery disease were equally represented. The entire series fell into these two groups with the exception of six patients with rheumatic heart disease and two the etiology of which was unknown.

*From the Medical Clinic of the Peter Bent Brigham Hospital.
†Aided by a grant from the Proctor Fund of Harvard University for the Study of Chronic Diseases.

Arterial hypertension existed in 81 per cent of those with coronary disease and in two of those with rheumatic heart disease, making a total of 83 per cent with arterial hypertension. The heart was clinically enlarged in 77 per cent. Symptoms and signs of myocardial insufficiency to a fairly marked degree were present in the majority. The functional state of the group as a whole was remarkably poor. The average duration of life after the detection of pulsus alternans was fourteen and one-half months.

Effect of Age.—Since the occurrence of alternation in young individuals is rare, it is not surprising that only five patients were under the age of forty years. In these the average duration of life after detection of the alternating pulse was about six months, less than half the general average. Patients at the other extreme of age, those of seventy years or more, lived almost nineteen months, three times as long as the youngest group, and considerably longer than the general average. Between these extremes there was a gradual increase in the length of life. The older the patient at the time alternation was detected, the longer the duration of life after detection. These and the other data are shown in Table I and Fig. 1.

TABLE I

	NUMBER OF CASES	AVERAGE DURATION OF LIFE		
		YEARS	MONTHS	DAYS
Total cases	71	1	2	13
Hypertensive cardiovascular disease	32	1	4	23
Coronary artery disease (including angina pectoris)	31	–	–	–
With coronary occlusion	9	0	5	19
Without coronary occlusion	22	1	5	13
Alternation appearing during acute infarction	5	0	1	15
Rheumatic heart disease	6	0	9	6
Unknown etiology	2	0	0	27
Age: Below 40 years	5	0	6	4
40 to 49 years	10	0	10	18
50 to 59 years	24	1	3	28
60 to 69 years	24	1	2	27
70 years or more	8	1	6	24
Sex: Males	50	1	4	29
Females	21	0	8	17
Total with hypertension	59	1	3	13
Total without hypertension	12	0	8	24
Systolic blood pressure: Below 120 mm.	4	0	1	6
120 to 149 mm.	16	1	0	2
150 to 199 mm.	21	1	10	15
200 mm. and above	30	0	11	27
Diastolic blood pressure: Below 90 mm.	8	0	10	9
90 to 99 mm.	9	2	2	7
100 to 119 mm.	26	1	6	3
120 mm. and above	28	0	7	27
Frank congestive failure	25	0	10	11
Without congestive failure	46	1	4	21
Intraventricular heart-block	14	2	2	10
Normal intraventricular conduction	19	1	4	13

Sex.—The average life, after discovery of pulsus alternans, of the fifty males was about seventeen months; of the twenty-one females, eight and one-half months. The prognosis, then, seemed to be twice as poor in females as in males.

Blood Pressure.—The average length of life after detection of pulsus alternans in the patients with arterial hypertension was fifteen and one-half months, while in those without it it was nine months. These figures became more striking when the blood pressure groups were

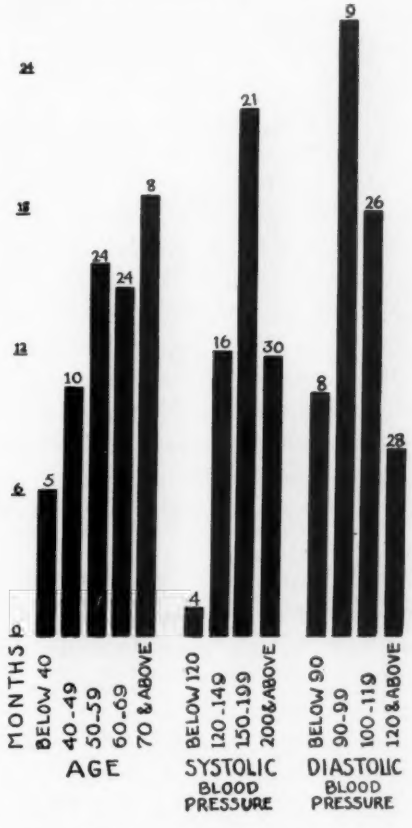

Fig. 1.—The figures at the top of each column indicate the number of cases represented.

more closely analyzed. There were four patients with systolic tensions below 120 mm. The average length of life in these was only slightly more than one month. The group with normal pressures of 120 to 149 mm. averaged one year of life. With a moderate elevation to 150 to 199 mm. the average was strikingly longer, almost twice as long as was the general average. With still higher tensions of 200 mm. or more the average fell again to about one year. The average length of life of patients with normal diastolic tensions was somewhat

shorter than that of the group as a whole. The same is true of those with markedly elevated tensions. Those with a slight elevation to 90 to 99 mm. lived almost twice as long as the general average, those with moderate elevations considerably longer than the general average. Here we find that the higher the pressure, either systolic or diastolic, the better the prognosis until very high pressures were reached, when the averages fell again. Because of the very great frequency of hypertension in patients with pulsus alternans, this relationship becomes important. Hewlett[3] has stated that the outlook in patients with alternation is better if the blood pressure is high. This is true according to our series until the pressure becomes very high.

Congestive Failure.—Patients with frank congestive failure at the time alternation was first found made up 35 per cent of the series. The average duration of life in them was about ten and one-half months. The remainder presented no congestive signs or only a few minor ones. These latter lived, on the average, about 60 per cent longer than did those with failure. A number of the patients grouped as having no failure did have failure later, but the contrast was made according to the findings at the time alternation was discovered. In some respects this was scarcely a fair comparison, since the prognosis in a patient with frank congestive failure, other things being equal, would obviously have been worse than in one without it, regardless of the presence of pulsus alternans. The fact remains, nevertheless, that the presence of congestive failure increased the gravity of this physical sign.

Coronary Artery Disease.—The patients with coronary artery disease without occlusion who developed alternation of the pulse lived an average of seventeen and one-half months, while those who had suffered occlusions lived but five and one-half months. Those who had alternation during the early hours or days following an acute coronary closure lived even a shorter time—one month and a half. While the prognosis in coronary disease is known to be variable, these figures indicate a much more rapid course when alternation is present than is generally the case without it. It is our impression that on more careful study pulsus alternans will be found to occur during the early days following acute coronary thrombosis and then be seen to disappear with recovery and that the patients in whom this happens may yet have a more favorable prognosis.

Intraventricular Heart-Block.—There were fourteen patients with defective intraventricular conduction among the thirty-three whose electrocardiograms were taken. These, after alternation appeared, lived more than 50 per cent longer than those known not to have such conduction defects. Intraventricular block, then, not only did not

increase the gravity of the entire picture, but actually seemed to make the outlook somewhat better. This same favorable influence of intraventricular block was shown by Eppinger and Levine[4] in a series of patients with angina pectoris.

SUMMARY AND CONCLUSIONS

Certain factors which seemed to have a bearing on the prognostic significance of pulsus alternans in a series of 71 patients have been analyzed. Only patients known to be dead were selected for this study. The average duration of life after the detection of alternation was fourteen and one-half months.

The younger the patient the worse the prognosis was found to be.

The subsequent duration of life in the males was twice that in the females.

Moderate elevation of either the systolic or diastolic blood pressure seemed to exert a protective influence, but the prognosis became worse again when the pressure was very high.

The prognosis was considerably worse when congestive failure was present at the time of detection of alternation than when it was absent.

The occurrence of pulsus alternans in coronary occlusion, particularly if it appeared during the early hours or days following an acute myocardial infarction, seemed to make the prognosis much more grave.

The patients with intraventricular heart-block lived longer by more than 50 per cent than did those without it.

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A CASE OF PARASYSTOLE SHEWING SIMPLE INTERFERENCE DISSOCIATION

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INTRODUCTION

ALTHOUGH normally the sino-auricular node acts as the pacemaker for the whole heart, governing the auricular rate and through the conducting tracts controlling the ventricles, instances are frequent in which the authority of the normal pacemaker is, as it were, called in question. One is familiar with the paroxysmal tachycardias, in which the cardiac rhythm is dominated by an ectopic centre emitting impulses at a high rate, against which the sinus rhythm is ineffective. Again, in conditions in which for some reason the normal pacemaker is out of action, either in experimental destruction of that region or in cases of vagal slowing, the A-V node may take over the function of pacemaker; in cases of A-V heart-block, likewise, centres low in the bundle below the level of the lesion are responsible for the impulse-production which guides ventricular activity. Less common, but of great interest, are those cases in which two independent rhythms simultaneously compete for control of the heart. The possibility of such a condition was first suggested by Wenckebach,[6] who proposed the name "pararrhythmia" for the condition. An essential condition of the coexistence of two centres elaborating rhythmic stimuli at different rates is that each should be protected from the other, so that the impulses from the faster working centre do not capture the rhythm by penetrating to the other and destroying the stimuli in process of elaboration there. Such a protective block around each centre *(Schutzblockierung)* was postulated by Kaufmann and Rothberger[3] in their description of parasystole, the particular variety of pararrhythmia to be dealt with in this paper. Given such a condition of protective-block, the simultaneous existence of two stimulus-producing centres in the heart, acting at different rates, and each sending impulses into the ventricular muscle at rhythmic intervals, results in the contractile tissues responding to first one, then the other of the pacemakers: the rhythms can only interfere with one another so far that an impulse from one may arrive to find the muscle

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already in contraction in response to an impulse emanating from the other, or still refractory after such a contraction; in short, the two rhythms will interact to produce what is known as an "interference dissociation." Of this there are many varieties, according to the location of the two pacemakers, their relative rates, the facilities for conduction from chamber to chamber, and the effects of the extrinsic cardiac nerves upon the rhythms of one or both when the centres lie in territory within the sphere of influence of these nerves (e.g., vagal action on centres lying above the ventricular level). "Parasystole" is the term applied to that particular form in which one centre is located in the ventricle, elaborating stimuli at a rate generally slower than the sinus rhythm, which is responsible for the competing second rhythm. The term was introduced in 1917 by Kaufmann and Rothberger, who described cases in which extrasystoles of ventricular origin occurred, scattered here and there, singly and in pairs, throughout long records, and which on analysis displayed the interesting feature that the longer intervals between extrasystoles were always simple multiples of the interval separating a pair of extrasystoles occurring in immediate succession. It was apparent that a second rhythm, elaborating stimuli at the rate whose value was given by these pairs of extrasystoles, could well be responsible for all the extrasystoles in the records. As early as 1912 it had been suggested by Fleming[2] that some such mechanism might be at work, and although his observations were limited to polygraph tracings, he suggested that in cases showing regularly recurring ventricular extrasystoles "the rhythmical production of stimuli at an abnormally irritable point in the ventricles may produce such rhythmic irregularities."

This conception of parasystole, as developed by Kaufmann and Rothberger,[3] Singer and Winterberg,[5] and by subsequent workers, has been vigorously attacked from many sides. A full account of the theory and of the criticisms levelled against it will be found in the review by Rothberger,[4] who picturesquely says that the first critics were inclined almost "to throw out the baby along with the bath water." In spite of many objections it appears that the theory affords a valuable means of analysing a certain proportion of cases of extrasystolic arrhythmia. The total number of cases submitted to adequate analysis is not large: Faltitschek and Scherf[1] in 1932 referred to only eleven cases from the literature (including five from their own paper) in which parasystole as a simple interference-dissociation had been established. It has been emphasized that all cases from which full material is available should be published in detail. It is never justifiable to base a diagnosis of parasystole on short records, in which chance coincidence can play so great a rôle; and as in most cases short records alone are available from patients displaying extrasystoles in the clinic, the dearth of adequate analyses is readily understood.

Even when this factor has been given full weight, however, parasystole seems to be in effect a comparative rarity, only a very small percentage of the clinical cases displaying extrasystoles being capable of explanation on this basis. The present case, appearing to fulfill all the criteria justifying the diagnosis, is reported because of the fortunate circumstance that a long continuous electrocardiographic record is available for analysis.

CASE REPORT

J. MacF., male, aged fifty-nine years, a seedsman's manager, was examined as an out-patient at Royal Infirmary, Edinburgh, on Dec. 4, 1933. About one month previously he had been awakened about 5 A.M. by intense pain behind the sternum, which radiated to the left arm and was accompanied by a choking sensation. The intensity of pain overshadowed everything, and the patient could give no clear account of other symptoms beyond stating that "he thought his last day had come." Five very severe attacks of pain were experienced in the space of an hour. The patient was then given amyl nitrite inhalations by his family physician, and went to sleep. There was no recurrence of pain during the two weeks following, for which period he was confined to bed.

Two months prior to this attack, he had had a minor seizure of a similar nature. While playing bowls he felt mild pain, "more a soreness than actual pain," across the chest, accompanied by a choking feeling; this was severe enough to prevent his resuming his game, but next day he played again without recurrence of his symptoms. The patient denied any breathlessness on exertion, but the presence of some dyspnea is indicated by his admission of inability to sing now, though formerly he had been a professional vocalist.

Since his major attack he has had intermittently a hot burning sensation behind the sternum, but no actual pain.

Examination.—Pulse, 64 per minute, irregular in time. Blood pressure 140/90. Radial arterial wall not unduly thickened. Heart: Apex beat in fifth space, 3½ in. from midsternal line. Both sounds were closed and faint. Irregularity was due to audible extrasystoles. X-ray examination showed no cardiac abnormality. Electrocardiographic records described below. Retinae showed early arteriosclerotic changes, no hemorrhages or optic neuritis. Wassermann reaction, negative.

The patient was seen again on Feb. 7, 1934. The burning sensation complained of on previous visit persisted, otherwise he felt well. Good colour, without cyanosis or edema. Pulse, 56 per minute, regular. Blood pressure, 170/110. Other findings as on previous occasion. When seen for the third time on May 1, 1934, the patient still complained of the substernal burning sensation but denied any real pain. Pulse while sitting and at rest was regular, rate 56 per minute. A simple exercise test was carried out, the patient being allowed to walk on the level till pain was experienced. Standing up raised the rate to 64, while walking 40 yards on the level raised it to 67 and extrasystoles began to appear. Blood pressure, 132/88. The exercise was continued till slight pain was produced, when extrasystoles were frequent. Electrocardiographic records were made before and after the exercise test, and are described below.

ELECTROCARDIOGRAMS

Dec. 4, 1933: A routine electrocardiogram (short record) showed a regular sinus rhythm interrupted by ventricular extrasystoles, occurring at times in pairs in immediate succession. The P-waves were upright in all leads, somewhat deformed in

Leads II and III. The P-R interval measured 0.2 second. QRS in all leads measured 0.1 second. In Lead I a very small Q-wave was followed by a slurred R 3 mm. high, and that by an S 3 mm. deep (Fig. 1). T was deeply inverted, S-T not displaced. In Lead II Q was absent; R was slurred and 5 mm. high, and S 8 mm. deep. S-T was not isoelectric. T showed a positive summit 3.5 mm. high followed by a small negative phase. In Lead III Q was absent; R was splintered and of low amplitude (2 mm.), while S was 5 mm. deep and somewhat slurred. S-T elevation to the extent of 1 mm. was present. T was high (5 mm.) and positive. The appearances suggested a coronary infarct (anterior type) of some weeks' duration. An interesting feature of the record is that where two extrasystoles appeared in immediate succession, the final deflections of the first were deformed by a superimposed P-wave: the succeeding P-wave preceded the second extrasystole by a short interval (about 0.1 second), and by measurement of P-P intervals on the

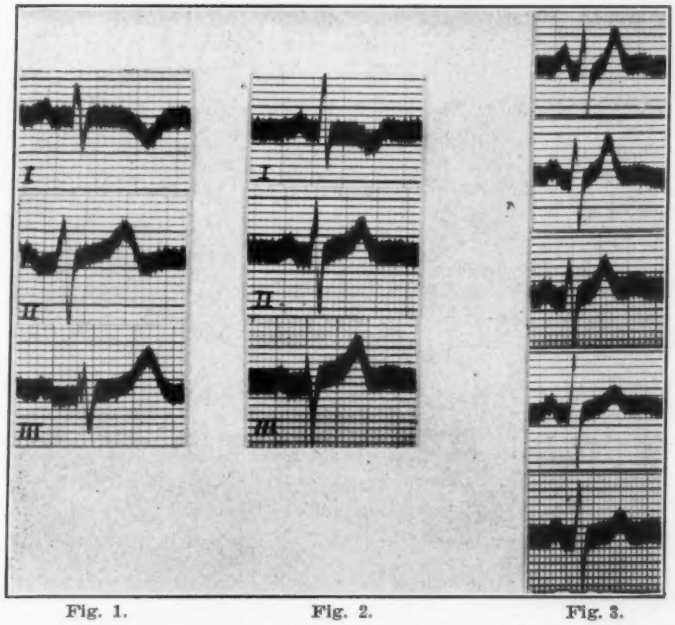

Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—Electrocardiogram, Dec. 4, 1933, Leads I, II, and III. In this and succeeding records time-marker is in fifths and twenty-fifths of a second, and standardisation is 1 cm. per millivolt.

Fig. 2.—Electrocardiogram, May 1, 1934, Leads I, II, and III.

Fig. 3.—Electrocardiograms, May 1, 1934, Lead II. The first record was taken immediately on cessation of exercise, the others at short intervals during the succeeding four minutes. Mild anginal pain was present when record 1 was taken.

curve it could be determined that rhythmic sinus impulses were responsible for all auricular deflections and that retrograde conduction was not responsible for those seen deforming the terminal deflections of the extrasystolic complexes.

Dec. 11, 1933: A short record in the three leads displayed similar features to that of a week before, although only single extrasystoles were then recorded. A film record taken on this date, however, displayed numerous extrasystoles, the analysis of which forms the basis of this communication (see below).

Feb. 6, 1934: Normal sinus rhythm, without extrasystoles. P-R interval still 0.2 second. Ventricular complexes of larger amplitude than in previous records, but of same general form. T in Lead I was more deeply inverted (–6 mm.), and

S-T in that lead depressed 1 mm. T-waves in Leads II and III were sharply positive. Such changes as had occurred from previous records were consistent with the original diagnosis of coronary infarct.

May 1, 1934: An electrocardiogram taken at rest showed features (Fig. 2) practically identical with those described Feb. 6, 1934, T in Lead I remaining sharply inverted, though smaller, T_2 and T_3, positive. Extrasystoles were absent. Following the exercise test referred to in the case report, serial electrocardiograms were made by Lead II over the space of several minutes. The rate rose from its resting value of 54 to 100 per minute and fell gradually to its original level on resting. The return to the slower rate was attended by the appearance of ventricular extrasystoles, which were similar in form to those recorded on previous occasions in this patient. Unfortunately, only short records, unsuitable for analysis, were secured. A striking change in the T-waves was noted in these records. The T-wave in Lead II before exercise measured +3 mm.; immediately after cessation of the exercise it measured +5 mm., and was markedly peaked in outline. A gradual return to the previous amplitude and form was observed in successive records (Fig. 3).

ANALYSIS OF FILM RECORD

Upward of 170 ventricular systoles were included in the film record obtained from the case, a portion of which is reproduced in Fig. 4, together with a diagrammatic representation of the probable mechanism involved. It will be seen from the electrocardiogram that a regular sinus rhythm is present, interrupted by ventricular extrasystoles scattered throughout the record, occurring singly and in pairs. When the intervals separating successive extrasystoles on the record are examined, they are found to be simple multiples of an interval approximating that which separates neighbouring extrasystoles occurring in immediate succession. For example, the interval between complexes *112* and *113* measures 138 × 0.01 second. (All measurements are in 0.01 second.) The interval between complexes *113* and *117*, the next succeeding extrasystole visible on the curve, measures 406, or three times 135.3. Similarly, the interval between complexes *117* and *122* measures 544, or four times 136; and the interval *108* to *112* measures 409, or three times 136.3. It is at once apparent that the extrasystoles do not occur haphazard, irregularly scattered through the record, but obey a rhythm whose fundamental period is about 135 to 138 hundredths of a second. If we draw in above the curve a scheme representing the sinus rhythm, and insert upon it arrows to represent a rhythm of the value found above, we see the mechanism clearly at once. When a stimulus of the second rhythm (the para-rhythm) falls during diastole, the ventricles respond by an extrasystolic contraction. When such a stimulus falls, however, during the systole of the ventricles, it is ineffective because of the refractory state of the ventricular muscle. All stimuli falling within a short period of the end of the T-wave are ineffective for a similar reason, the ventricle being relatively refractory for some little time after T is written (see below, under "Refractory Period"). At sev-

eral points on the record, para-stimuli fall at a time when a supraventricular stimulus is due; for example, the next para-stimulus after that which produced complex *108* falls approximately 0.3×0.01 second after the normal stimulus arriving from the A-V bundle is due. When we look at the electrocardiogram, we find that complex *109* is in effect intermediate in form between the extrasystolic form *(108)* and the

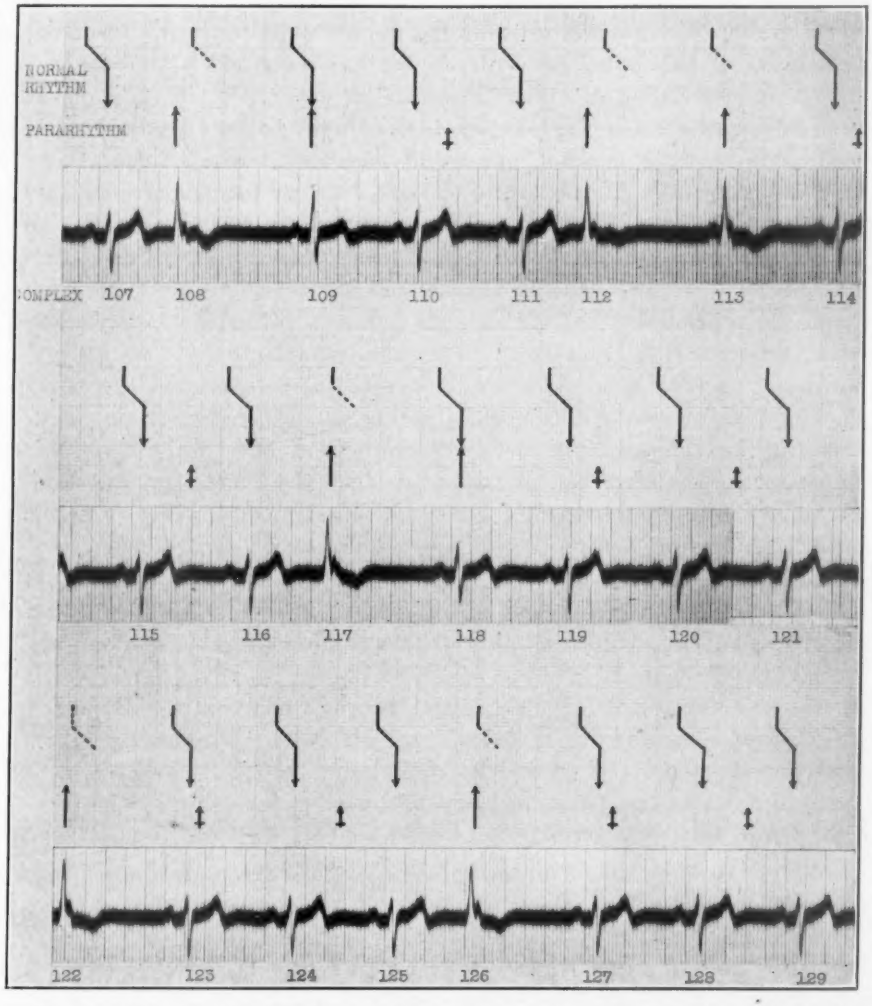

Fig. 4.—Electrocardiogram, Lead II; complexes *107* to *129* from the film record made on Dec. 11, 1933. The scheme above the record represents the interplay of the two rhythms. (See text and Table I.)

normal form *(110);* it appears that the two stimuli emanating from different points have met in the wall of the ventricles and have combined to produce a "mixed complex," analogous to those produced experimentally by Wilson and Herrmann.[7] These authors found that when the branch of the His bundle supplying one of the ventricles in

the dog had been cut, rhythmic stimulation of the ventricle supplied by that branch at a rate faster or slower than the sinus rate led to the appearance of "mixed complexes," transitional between those characteristic of stimulation of that ventricle and the opposite type produced by sinus beats with bundle-branch block affecting the conduction tissue to the side in question. In their case a well-timed stimulus, so released that the impulse from the auricle reached one ventricle via the intact branch of the bundle simultaneously with the activation of the opposite ventricle by the electrical stimulus, produced by summation of effects a normal complex. So in the present case, activation from the para-centre occurring simultaneously with activation from the normal supraventricular centre produces a type of complex intermediate between the two extreme forms characteristic of activation from either centre alone. Complex *109* is not alone in this configuration in the record reproduced: complex *118* is also intermediate in form between the normal and the extrasystolic types, and from the scheme we find that a para-stimulus falls 4.0×0.01 second after the normal beat is due. In the case of complex *113* we see immediately before it a rhythmic P-wave; the P-R interval is much shorter than normal (0.1 second), and it is apparent that the para-stimulus has already produced its full effect before the rhythmic stimulus arrives from the A-V bundle. The rhythmic stimulus, finding the ventricles already in contraction, is rendered ineffective in the same fashion that many of the para-stimuli are frustrated. We have in the record reproduced, therefore, evidence of simultaneous presence in full activity of two independent rhythms whose basic intervals bear no simple relation one to another (sinus rhythm about 56 per minute, para-rhythm about 44 per minute), and whose impulses interfere on occasion in the course of their spread through the ventricular muscle to produce complexes of mixed form. Before the diagnosis of para-systole with simple interference can be made absolute, analysis of a longer curve is necessary, and we will now proceed to consider the film record in its entirety.

Table I is modelled on those published by Singer and Winterberg,[5] and some explanation of its arrangement is necessary. The table is divided into sections by horizontal lines, each section containing from one to seven rows of figures. Starting from the first extrasystole on the record, the consecutive ventricular complexes have been numbered serially, and these numbers appear in the first column of the table. In the second column is the time interval between each complex and that preceding, irrespective of whether the complex be normal or extrasystolic. (All intervals are in hundredths of a second; these have been measured approximately from the curve, on which time markings were in $\frac{1}{25}$ and $\frac{1}{5}$ seconds. Comparator readings were not used, being considered unnecessary for the present purpose.) The

last complex in each section is an extrasystole: where only one complex occurs between a pair of lines, it is the second of a pair of extrasystoles occurring in immediate succession (e.g., complex *2*, complex *113*). The figures in the third column are the measured intervals from any normal complex to the last preceding extrasystole; e.g., the figure 220 opposite complex *115* indicates that complex *115* occurred 220 × 0.01 second after the last preceding extrasystole, complex *113*. Similarly, in the fourth column are found corresponding values for the extrasystolic complexes: the extrasystole *117* occurs 406 × 0.01 second after the preceding extrasystole *113*. The italicised figures in the fifth column indicate the interval separating any extrasystole from the last preceding normal beat, the "manifest coupling." In the sixth column are found the average values for the sinus-rhythm interval for each section, while in the last column are the average values for the para-rhythm intervals, as calculated by dividing the figures in column 4, by the number of para-intervals included in the section. For example, the section *114* to *117*, which is figured in Fig. 4, contains three para-cycles, whose average value is thus 135.3 (3 × 135.3 = 406). There remain to be explained the nonitalicised figures in column 5. These are the "latent couplings" and are calculated as follows: Having found the average para-interval for each section, we calculate what relation each para-stimulus must bear to the stimuli of the normal supraventricular rhythm. Complex *114*, for example, falls 114 × 0.01 second after the extrasystole *113;* a para-stimulus is due 135.3 × 0.01 second after that extrasystole, that is, 21.3 × 0.01 second after the normal beat *114*. We may enter that figure 21.3 in column 5 as a "latent coupling," indicating where an extrasystole would have occurred had the ventricle not been refractory. Similarly, another para-stimulus was due at 2 × 135.3 after complex *113*, that is 270.6 after that extrasystole. The normal beat *115*, however, fell at 220 after complex *113*, so again the para-stimulus was frustrated, falling 50.6 hundredths of a second after the ventricle had passed into contraction. We enter 50.6 as the latent coupling for complex *115*—and so on. Certain of the latent couplings are very short, between 0.3 and 0.04 or 0.05 second; a few are entered as negative quantities of small magnitude. These indicate that a para-stimulus and a normal stimulus fell very nearly together; according to our theory, such should result in "mixed beats." The asterisks opposite certain of the figures in column 5 indicate such mixed complexes as are actually visible on the record, and it will be noted how closely observation accords with theory in this respect. (See also below, "Combination Complexes.")

Consideration of the table shows that a para-rhythm can be postulated which will account for the observed phenomena throughout. The occurrence of the mixed or combination complexes is strong corroborative evidence of the simultaneous presence of two rhythms.

TABLE I

COMPLEX NUMBER	CONSECUTIVE VENT. CYCLES	NORMAL BEATS: OCCURRENCE	EXTRASYSTOLES: OCCURRENCE	COUPLINGS	AVERAGE CYCLE (NORMAL RHYTHM)	AVERAGE CYCLE (PARARHYTHM)
1	66		66	*66*		
2	130		130			130
3	114	114		18.6		
4	102	216		49.2	103.4	132.6
5	98	314				
6	84		398	*84*		
7	119	119		12		
8	92	211		51	101	131
9	96	307				
10	86		393	*86*		
11	112	112		29.2		
12	100	212		70.4		
13	100	312				
14	100	412		11.6	102.5	141.2
15	102	514		51		
16	102	616				
17	90		706	*91*		
18	114	114		34		
19	100	214			98	148
20	82		296	*82*		
21	112	112		35		
22	98	210			96	147
23	84		294	*84*		
24	106	106		37		
25	100	206			100	143
26	80		286	*80*		
27	120	120		22		
28	102	222			101.3	142
29	62		284	*62*		
30	140	140		–3*		
31	102	242		44.6	102	143.3
32	102	346				
33	84		430	*84*		
34	120	120		23		
35	106	226			105.3	143
36	60		286	*60*		
37	150	150		–6*		
38	108	258		30	105.5	144
39	108	366				
40	66		432	*66*		
41	140	140				140
42	108	108		34		
43	104	212			103	142
44	72		284	*72*		
45	128	128		13.3		
46	106	234		48.6	106	141.3
47	106	340				
48	84		424	*84*		
49	128	128		13.6		
50	108	236		49.2	106.8	141.6
51	110	346				
52	79		425	*79*		
53	130	130		10.6		
54	104	234		47.2	102	140.6
55	102	336				
56	86		422	*86*		

TABLE I—CONT'D

COMPLEX NUMBER	CONSECUTIVE VENT. CYCLES	NORMAL BEATS: OCCURRENCE	EXTRASYSTOLES: OCCURRENCE	COUPLINGS	AVERAGE CYCLE (NORMAL RHYTHM)	AVERAGE CYCLE (PARARHYTHM)
57	116	116		26		
58	100	216			100	142
59	68		284	*68*		
60	132	132		6.6		
61	100	232		45.2	100	138.6
62	98	330				
63	86		416	*86*		
64	116	116		20.6		
65	100	216		57.2	105	136.6
66	106	322				
67	88		410	*88*		
68	126	126		7.6		
69	103	229		38.6	104.8	133.6
70	104	333				
71	68		401	*68*		
72	134	134		2.6		
73	100	234		39.2	100.5	136.6
74	102	336				
75	74		410	*74*		
76	126	126		12		
77	104	230		46	105	138
78	106	336				
79	78		414	*78*		
80	132	132		5.8		
81	112	244		31.5		
82	112	356		57.3	113.8	137.8
83	110	466				
84	85		551	*85*		
85	136	136		2		
86	110	246		30	105	138
87	106	352				
88	62		414	*62*		
89	142	142				142
90	110	110		32.5		
91	102	212			105.5	142.5
92	73		285	*73*		
93	136	136		5.3		
94	104	240		42.6	105	141.3
95	106	346				
96	78		424	*78*		
97	132	132		10		
98	106	238		46	107	142
99	110	348				
100	78		426	*78*		
101	134	134		8*		
102	112	246		38	107	142
103	108	354				
104	72		426	*72*		
105	136	136		2.6*		
106	106	242		35.2	104	138.6
107	106	348				
108	68		416	*68*		
109	136	136		0.3*		
110	104	240		32.6	102.8	136.3
111	104	354				
112	65		409	*65*		

TABLE I—CONT'D

COMPLEX NUMBER	CONSECUTIVE VENT. CYCLES	NORMAL BEATS: OCCURRENCE	EXTRASYSTOLES: OCCURRENCE	COUPLINGS	AVERAGE CYCLE (NORMAL RHYTHM)	AVERAGE CYCLE (PARARHYTHM)
113	138		138			138
114	114	114		21.3		
115	106	220		50.6	107.6	135.3
116	108	228				
117	78		406	*78*		
118	132	132		4*		
119	110	242		30		
120	108	350		58	107.2	136
121	108	458				
122	86		544	*86*		
123	124	124		12		
124	102	226		46	102	136
125	104	330				
126	78		408	*78*		
127	126	126		11.3		
128	102	228		46.6	102	137.3
129	102	330				
130	82		412	*82*		
131	122	122		15.3		
132	104	226		48.6	105	137.3
133	102	228				
134	84		412	*84*		
135	130	130		18		
136	106	236		60		
137	104	340				
138	108	448		–4*	107.1	148
139	108	556		36		
140	110	666				
141	74		740	*74*		
142	139		139			139
143	105			22.3		
144	102	207			101.3	137.3
145	68		275	*68*		
146	130	130		5.3*		
147	96	226		44.6	98	135.5
148	98	324				
149	82		406	*82*		
150	116	116		20		
151	98	214		56	104.5	136
152	106	320				
153	88		408	*88*		
154	126	126		28		
155	108	234		74		
156	108	342			108.3	154
157	106	448		14		
158	105	553				
159	63		616	*63*		
160	142	142		–4*		
161	102	244		30	101.8	138
162	100	344				
163	70		414	*70*		
164	123	123		7.3		
165	98	221		39.6	101	130.3
166	96	317				
167	74		391	*74*		

*Mixed complexes actually visible on the record. (See text.)

The para-intervals in Table I show variation between extreme values of 130 and 154: the majority of transitions occur gradually, and there are but three instances in the whole record where sudden variations amounting to 4×0.01 second or more occur. [These instances are (a) between complexes *10* and *18*, where the intervals lengthen from 131 to 148×0.01 second; (b) between complexes *134* and *142*, where the para-interval temporarily lengthens from 137.3 to 148, returning again to 139×0.01 second; and (c) between complexes *153* and *160*, where the para-intervals again temporarily lengthen from 136 to 154 hundredths of a second.] The first and third of these sudden variations are the subject of discussion below, under the head "Latent Couplings"; the second is interesting in that a mixed complex occurs in the middle of the section with the slower pararhythm, and that in a position predictable from the table (complex 138), so that the calculated para-intervals are in this instance substantiated by direct observation.

Refractory Periods.—In their original papers on the subject, Kaufmann and Rothberger took as a measure of the refractory period the duration of QRST—i.e., the absolute refractory period. It was later suggested by Singer and Winterberg that this might not represent the actual effective refractory period; a state of partial refractoriness supervenes at the end of the absolute refractory phase, and it is possible that the ventricle may persist in a refractory state for some little time after the end of T, at least so far as stimuli of the strength of those emanating from our hypothetical "para-centre" are concerned. As we have no measure of the strength of these stimuli and no means of testing the ventricular refractory period directly, we must have recourse to indirect methods. It was suggested by Singer and Winterberg that if one found a "latent coupling" which consistently failed to produce an extrasystole, and close to it in magnitude a "manifest coupling" which consistently was followed by an extrasystole, then the refractory period for stimuli of the particular strength here concerned must lie between these two values. On examination of Table I we note that the "latent couplings" of 57.2 (complex *65*) and 57.3 (complex *82*), 58 (*120*) and 60 (*136*), are not followed by responses; while the "manifest couplings" 60 (complex *36*) and 62 (complexes *29* and *88*) are followed by extrasystoles. The relative refractory period, therefore, by this method, lies between 57.3 and 62 hundredths of a second, probably close to 60×0.01 second.

Scrutinising the column of "couplings" with this value for the refractory period as standard, we find that with two exceptions all couplings above the value of the refractory period are "manifest," i.e., whenever a para-stimulus falls late enough in diastole to be outside the relative refractory period, an extrasystole results. The two

exceptions are complexes *12* and *155*, with "latent" couplings of 70.4 and 74, respectively. The explanation of this inconsistency will be discussed below. (See "Exit-block.")

"*Exit-Block.*"—Of the various auxiliary theories which have been introduced as part of the theoretical superstructure erected upon the simple conception of parasystole as we have so far defined it, that of *Austrittsblock* has perhaps given rise to most controversy. By the term, which we may translate as "exit-block," the idea is conveyed that certain of the impulses arising in the para-centre are unable to pass out freely into the neighbouring muscle, and that a condition of block exists between para-centre and muscle comparable to that produced between auricle and ventricle by lesions of the auriculoventricular bundle. The necessity for such an hypothesis arises in some cases of apparent parasystolic rhythm in which frequent para-stimuli fall during ventricular diastole outwith the relative refractory period, without ventricular extrasystoles appearing in the record. A close parallel with A-V block is provided by these instances (Singer and Winterberg[5]) where the para-rhythm as measured directly between a pair of extrasystoles occurring in immediate succession is slightly longer than that calculated from subdivision of long intra-extrasystolic intervals, as though the second emerging impulse had been delayed in similar fashion to prolongation of the P-R interval in first stage of A-V heart-block. It finds its main application, perhaps, in the explanation of certain cases of paroxysmal tachycardia, in which the records between attacks display extrasystoles of the same form and presumably the same origin as the complexes constituting the paroxysms, and the intervals between the extrasystoles are simple multiples of that separating the complexes during a paroxysm. An obvious explanation for such a condition is to postulate a rhythmic para-centre, whose activity persists at the same high rate irrespective of whether a paroxysm is or is not present: during a paroxysm each stimulus elaborated in the centre reaches the ventricular muscle and each produces a response, the high inherent rate of the ectopic centre being sufficient to ensure its capturing the rhythm. Between paroxysms, on the other hand, the presence of some degree of "exit-block," sufficient to prevent most of the stimuli from reaching the muscle while allowing an occasional impulse to escape, would account for the observed regular sinus rhythm broken by occasional extrasystoles of similar form to those constituting the paroxysm, whose spacing indicates that they belong to the same fundamental rhythm as the beats in a paroxysm. Cases have been described where "exit-block" has to be postulated in the analysis of a parasystole case such as we here describe, in the absence of paroxysmal tachycardia, and this is especially so when the absolute refractory period, as calculated from the duration of QRST, is taken as a measure of the lowest permissible

coupling, instead of the relative refractory period calculated by the method of Singer and Winterberg detailed above. Cases in which the relative refractory period is taken into account, and which still necessitate exit-block as an auxiliary, are generally those where the para-rhythm is faster than the sinus rhythm. (Faltitschek and Scherf.[1])

In the analysis of the case under consideration, there are but two instances where a "para-stimulus" falls in diastole outwith the refractory period of the ventricles, and no response is apparent in the record. In Table I these long couplings without manifest responses occur in the cycles *12* and *155*. The nonappearance of extrasystoles in these cycles could be explained on any one of four grounds: (1) a rhythmic para-stimulus was not elaborated at that time; (2) the ventricle was still refractory when the stimulus arrived; (3) the stimulus was of lower intensity than usual; or (4) "exit-block" was present and the elaborated stimulus did not reach the ventricle. The second and third possibilities may be considered together, since we are dealing with the relative refractory period, whose duration depends closely on the strength of stimulus concerned. It might be that a stimulus of lowered intensity had been elaborated, to which the ventricle remained refractory, a possibility we have no means of proving or disproving; that the refractory period to a stimulus of similar intensity to the other para-stimuli should in this particular instance be prolonged seems highly improbable. The "exit-block" hypothesis would obviously afford a simple explanation, but we are faced with the problem why in these particular cycles the emerging para-stimuli should have been obstructed, when in the other fifty instances in the record in which a para-stimulus fell during the non-refractory phase, no such exit-block was apparent. The first possibility, that a para-stimulus was not elaborated at that precise moment, demands further consideration. It will be noted from a scrutiny of Table I that in both cases when such a long "latent coupling" occurred there was a coincident and abrupt transition in the rhythm of the para-centre from a faster to a slower rate. For example, over the cycles *7* to *10* the para-rhythm interval averaged 131 × 0.01 second; over the cycles *3* to *6*, 132.6 hundredths second; and for the directly measurable cycle *1* to *2*, 130 hundredths second. The long latent coupling occurred during the section including cycles *11* to *17*, where the average para-rhythm cycle averaged 141.2 × 0.01 second. The average para-rhythm cycle for section *18* to *20* was 148 × 0.01 second; for cycles *21* to *23*, 147 × 0.01 second, and for cycles *24* to *26*, 143 × 0.01 second. A sudden transition from a shorter para-rhythm interval to one longer by 17 × 0.01 second therefore occurred during the section including cycles *11* to *17*. Similarly, in the other instance of long latent coupling, the directly measured para-interval for cycle *142* measured 139 × 0.01 second; for cycles *143* to *145* it averaged 137.3 × 0.01

second; for cycles *146* to *149*, 135.5 × 0.01 second; for cycles *150* to *153*, 136 × 0.01 second. For the section including the long latent coupling (*154* to *159*) the para-interval averaged 154 × 0.01 second; for the succeeding cycle *159* to *160* it was measured as 138 × 0.01 second; and for cycles *161* to *163* it averaged 138 × 0.01 second. Again the section including the abnormally long latent coupling was one of transition from short to longer para-interval. In the computation of the latent couplings in the table it has been assumed that the para-rhythm over the whole of a section remained constant at its average value for that section, and that when transitions occurred they did so suddenly in the cycles demarcating sections—both assumptions that are in fact highly improbable. If we assume, as is much more likely, that transitions occurred gradually over the space of several para-cycles, then recalculation of the latent couplings for these sections is necessary, the effect being to shift the earlier couplings somewhat forward and thus to shorten those which appear abnormally long in the original table.

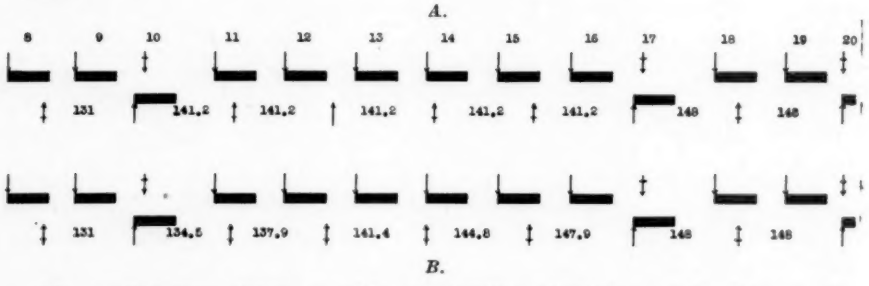

Fig. 5.—Diagrams drawn to scale, representing alternative relationships of the two rhythms between cycles *8* to *20* of the film record. In each diagram the upper row of downwardly directed arrows indicates the successive ventricular responses to supraventricular impulses. The lower row (upwardly directed) indicates the para-rhythm stimuli. Black rectangles indicate the times during which the ventricles are refractory, and crossed arrows of either series indicate stimuli ineffective through falling during these refractory periods.

In Fig. 5*A* the para-interval is supposed to increase abruptly from 131 to 141.2 x 0.01 sec., remaining at that value for five cycles before increasing further to 148. The fourth para-stimulus is seen to fall outwith the ventricular refractory period, without producing a response.

In Fig. 5*B* the para-interval is drawn as increasing by equal increments from 131 to 148 x 0.01 sec. The anomalous para-stimulus is now seen to fall within a period of ventricular refractoriness.

In Fig. 5 the effect of such a modification of the calculated para-rhythm intervals upon the latent couplings in cycles *8* to *10* is shown diagrammatically. When the transition from fast to slower rhythm is assumed to occur abruptly, the time relations of the para-stimuli to the ventricular refractory periods are as shown in Fig. 5*A*; an obvious discrepancy is notable in cycle *12* to *13*, in which a para-stimulus falls outwith the refractory period without provoking a response. On the other hand, when a gradual but regular increase in the successive para-intervals is assumed to occur, each interval from that succeeding complex *10* being longer than its predecessor by 3.45 × 0.01 second,

till the value 147.9 is reached in the cycle preceding complex *17*, the long latent coupling in question is materially shortened (Fig. 5*B*).

In the other series (complexes 154 to 159), such a modification of the calculated para-rhythm does not entirely obviate the difficulty. The para-rhythm here has the following values: 2×137.5; 3×134.5; 3×136; 4×154; 3×138. The long para-interval is in this case not maintained after the group *154* to *159*, but falls at once to the old value of around 137-138 × 0.01 second. Assuming that the transition to a longer interval occurred gradually and that the return was also gradual, all in the space of four para-cycles, one must assume a very high value (circa 175 × 0.01 second) for the longest cycle, if the average of 154 × 0.01 second for the whole group is to be maintained. This seems unwarranted, unless some other mechanism can be shown (or postulated) to account for the long cycle. A feasible explanation is the possibility of momentary failure of the protective block *(Durch-*

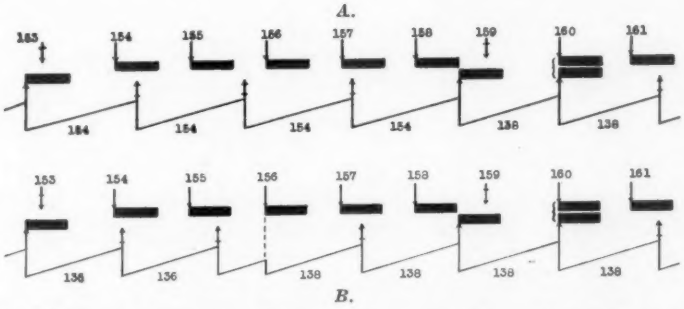

Fig. 6.—Diagrams drawn to scale as in Fig. 5, with the addition of a scheme indicating the building-up of the impulses in the ectopic centre. Cycles *153* to *161* are represented. (See Table I.)

In Fig. 6*A*, where the para-rhythm is shown as 154 × 0.01 sec. for four cycles, then returning to 138, the third para-stimulus falling between complexes *155* and *156* provokes no response.

In Fig. 6*B* the anomaly is seen to be obviated if the supraventricular impulse *156* penetrates to the para-centre and destroys the impulse in process of elaboration. The para-interval remains practically constant at 136-138 × 0.01 sec.

bruch der Schutzblockierung) which is represented diagrammatically in Fig. 6. The upper of the two diagrams in that figure shows the mechanism if the para-rhythm be assumed to increase from 136 to 154 × 0.01 second for five cycles: cycle *155-156* shows the para-stimulus falling late in diastole without ventricular response, which demands explanation. In the lower diagram is shown the alternative mechanism. The para-centre is shown elaborating impulses at intervals of 136 × 0.01 second. The sequential complex *156* is assumed to penetrate the exit-block and destroy the stimulus in process of elaboration so that the para-centre must begin again to elaborate a stimulus from the beginning. From the diagram it is clear that if stimulus production goes on at practically the old rate (138 × 0.01 second instead of

136), the appearance of the subsequent extrasystoles *159* and *160* can be accounted for without difficulty.

It is not claimed that these explanations represent beyond all doubt the mechanism involved; they are put forward for consideration only, as alternatives to the assumption of *Austrittsblock* in the explanation of the long latent couplings. Their acceptance or rejection does not materially affect the conclusion that the case is one of parasystole with interference, since in the long record analysed these intervals alone are paradoxical; and the evidence of a second "interfering" para-rhythm is conclusive (divisibility of intervals and presence of all grades of transition complexes). One must emphasise, as has been done by Rothberger, that it is not to be expected that a record from a clinical case will conform with mathematical accuracy to our analysis. Even under experimental conditions, where the "para-centre" is replaced in the dog heart by rhythmic stimuli from an electric contrivance, conformity to law is not absolute. The variations possible under clinical conditions are manifold and incalculable, and in analysis one is faced with that element of uncertainty inherent in biological work as contrasted with that employing physicochemical systems of less complexity under controllable conditions.

Combination Beats.—In Fig. 7 is reproduced a series of complexes illustrating the various forms of combination beats encountered in the record. The first complex of each pair is always a frank extrasystole; the second is a "mixed beat" showing combination of the two impulses in varying time relations. In Fig. 7*A* the second complex is of pure extrasystolic form: a P-wave is visible preceding the ventricular complex by 0.1 second, and it is apparent that the para-stimulus has forestalled the supraventricular stimulus by the difference between this interval and the usual P-R found before normal complexes elsewhere in the record, that is by 0.1 second. The last pair of complexes figured (Fig. 7*H*) depicts an extrasystole followed by a normal supraventricular complex, the latent coupling in this instance being 18×0.01 second. Between these two extremes all gradations are met with in the record. The second complex of Fig. 7*B* closely approximates to the extrasystolic form; here again a P-wave is visible, but P-R in this instance is 0.16 second: the para-stimulus precedes the supraventricular by only 0.04 second, and some interference has taken place. In Fig. 7*C* the P-R of the second complex is normal (0.2 sec.), and the ventricular complex shows further modification, particularly in the depth of S and in the sign of the T-wave. Actually from Table I it will be noted that the latent coupling for this complex was calculated at -4×0.01 second. The second complexes in *D*, *E*, *F* and *G* of the same figure show progressive modification of the ventricular com-

plexes in the direction of the normal supraventricular type: the latent couplings as calculated for these complexes are respectively –3; 4; 2.6; and 5.3 × 0.01 second. There is thus close correspondence between the form of the mixed complex and the relation of para- and supraventricular stimuli to one another.

Couplings.—The manifest couplings in the table have been examined with a view to determining whether these showed any tendency for the extrasystoles to occur at a particular point in diastole, or whether

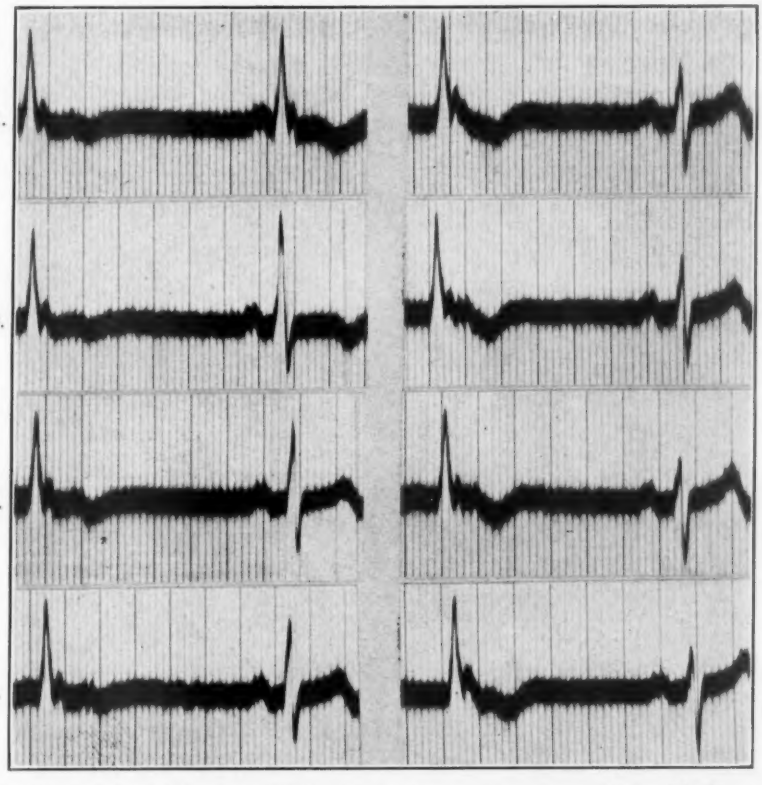

Fig. 7.—Electrocardiograms, Lead II, showing various forms of "combination complexes" from pure extrasystole (7*A*) to pure supraventricular (7*H*). The bracketed figures below indicate the time relation of R of the second complex of each pain to "R" of the expected sequential beat, calculated as in Table I. All values in 0.01 second.

7*A* Complexes *112-113* (–10)
7*B* Complexes *141-142* (–4)
7*C* Complexes *159-160* (–4)
7*D* Complexes *29-30* (–3)
7*E* Complexes *117-118* (+4)
7*F* Complexes *104-105* (+2.6)
7*G* Complexes *145-146* (+5.3)
7*H* Complexes *134-135* (+18)

they occurred scattered evenly throughout that interval. In Fig. 8 the results of the examination are depicted schematically, abscissae representing the various lengths of coupling, and ordinates the number of times each coupling occurred. It will be seen that all couplings lie in the period from 60 to 91 × 0.01 second after the preceding systole. The lower limit of this period we have seen to coincide with the

end of the relative refractory period: the upper limit is not clearly defined. Combination complexes have been omitted from this analysis: had they been included we would have had a fresh series of ordinates, 10 in all, distributed in the region of 99 to 114. There would still be a considerable gap between 91 and 99 without manifest couplings. The distribution of the couplings between 60 and 91 is seen to be fairly even, with some increased frequency in the region of 77 to 85.

SUBSEQUENT EXAMINATION

The patient again reported for examination on March 1, 1935, fifteen months after his first visit. He was in fair health but still complained of precordial discomfort on exertion. Physical examination revealed no significant alteration in the signs since examination a year before.

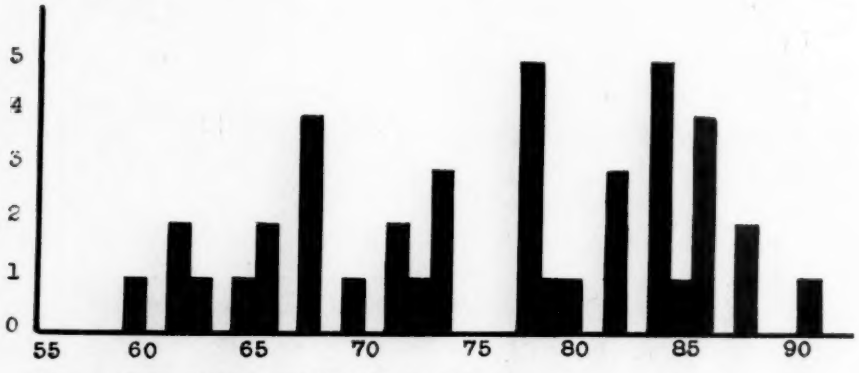

Fig. 8.—Graph showing distribution of couplings.
Abscissae: Coupling in hundredths of a second.
Ordinates: Number of instances each value occurred.

Electrocardiogram was made by Lead II after exercise. This film record, comprising 217 ventricular complexes, displayed normal rhythm with an initial rate of 112 per minute. After 68 seconds one ventricular extrasystole occurred, the rate having fallen to 66 per minute. One minute later the rate remaining approximately constant, ventricular extrasystoles were frequent. The T-waves showed similar changes to those described above (see record of May 1, 1934); the amplitude of T immediately after exercise was 7 mm., thirteen seconds later it was 8 mm., falling gradually to 5 mm. at 120 seconds.

The extrasystoles were of strikingly similar form and distribution to those in the record already analysed. Their spacing suggested the possibility of a "para-rhythm," and the record was examined critically to determine whether this was so. Measurements were made from the curve embracing all but the first isolated extrasystole and are given in Table II, which has been compiled in similar fashion to Table I.

It will be seen that a para-rhythm of slow rate can be demonstrated in this curve. The para-rhythm shows no sudden variations, all changes being gradual. The cycles shorten from an initial value of 149 × 0.01 second, to a minimum of 135 × 0.01 second, gradually increase again to 144 × 0.01, and finally shorten to 139 × 0.01 second at the end of the record. One mixed or combination complex occurs in the record (complex 17 of Table II), and this is reproduced in Fig. 9. It occurs at a point where by calculation normal and ectopic beats fall precisely together, and corresponds in form to the combination complex in Fig. 7*E*.

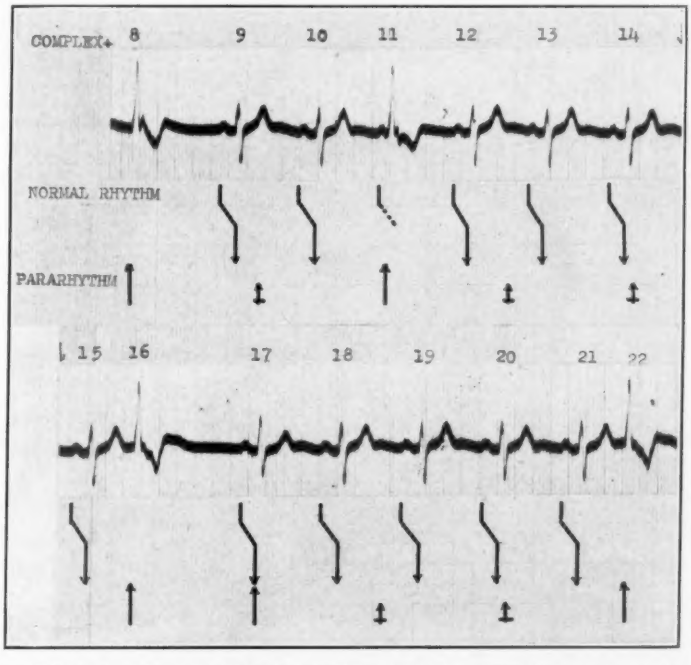

Fig. 9.—Electrocardiogram, March 1, 1935, Lead II. Complexes 8 to 22 of the film record made fifteen months after the original records. The scheme below the record represents the interplay of the two rhythms. (See text and Table II).

The shortest manifest coupling in the record was 52 × 0.01 second, which occurred four times. The longest latent coupling was 56 × 0.01 second, occurring once only. No other latent coupling exceeded 50 × 0.01 second. With one exception, therefore, all para-stimuli falling out with the relative refractory period produced ventricular responses, and that period in this record appears to be over 49 and under 52 × 0.01 second.

It seems justifiable, therefore, to conclude that a similar para-rhythm was present when this record was made. From the form of the extrasystolic complexes the ectopic focus would appear to be the

end of the relative refractory period: the upper limit is not clearly defined. Combination complexes have been omitted from this analysis: had they been included we would have had a fresh series of ordinates, 10 in all, distributed in the region of 99 to 114. There would still be a considerable gap between 91 and 99 without manifest couplings. The distribution of the couplings between 60 and 91 is seen to be fairly even, with some increased frequency in the region of 77 to 85.

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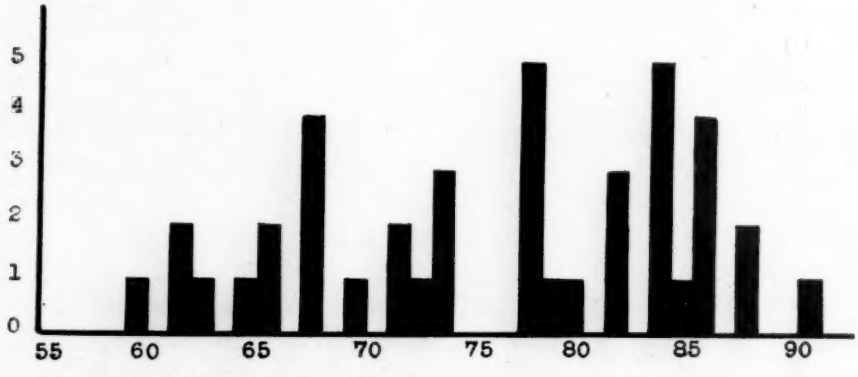

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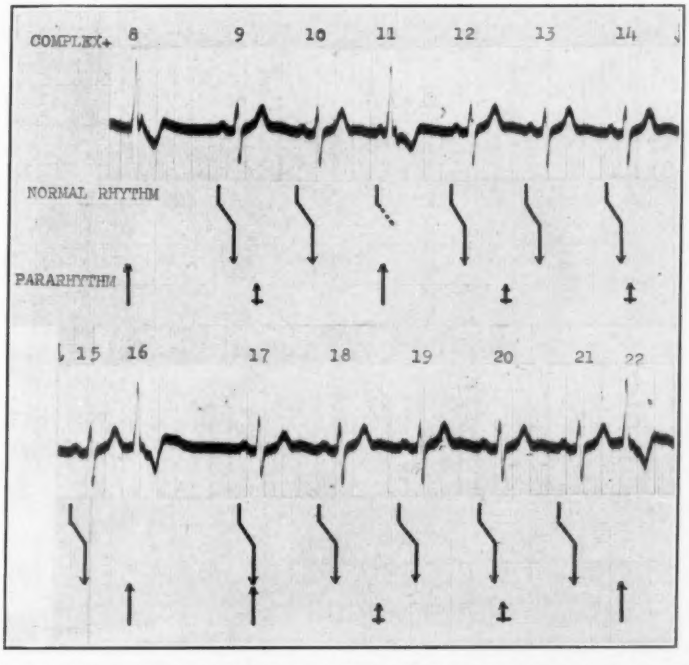

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It seems justifiable, therefore, to conclude that a similar para-rhythm was present when this record was made. From the form of the extrasystolic complexes the ectopic focus would appear to be the

TABLE II

COMPLEX NUMBER	CONSECUTIVE VENT. CYCLES	NORMAL BEATS: OCCURRENCE	EXTRASYSTOLES: OCCURRENCE	COUPLINGS	AVERAGE CYCLE (NORMAL RHYTHM)	AVERAGE CYCLE (PARARHYTHM)
1	68		68	*68*		
2	100	100		49		
3	80	180				
4	84	264		34		
5	80	344			85	149
6	86	430		37		
7	94	524				
8	72		596	*72*		
9	116	116		28		
10	92	208			92	144
11	80		288	*80*		
12	92	92		46.6		
13	84	176				
14	92	268		9.2	90.6	138.6
15	96	364				
16	52		416	*52*		
17	138	138	138	*138*		
18	92	230		46		
19	90	320			90.5	138
20	90	410		4		
21	90	500				
22	52	552	552	*52*		
23	128	128		10		
24	88	216			88	138
25	60		276	*60*		
26	114	114		22		
27	86	200			86	136
28	72		272	*72*		
29	104	104		31		
30	88	192			88	135
31	78		270	*78*		
32	108	108		28		
33	94	202			94	136
34	70		272	*70*		
35	120	120		16		
36	94	214			94	136
37	58		272	*58*		
38	128	128		10		
39	96	224			96	138
40	52		276	*52*		
41	134	134		8		
42	94	228			94	142
43	56		284	*56*		
44	130	130		12		
45	92	222			92	142
46	62		284	*62*		
47	132	132		12		
48	100	232		56	100	144
49	104	336				
50	96		432	*96*		
51	112	112		25		
52	94	206			94	137
53	68		274	*68*		
54	134	134		8		
55	98	232			98	142
56	52		284	*52*		

TABLE II—CONT'D

COMPLEX NUMBER	CONSECUTIVE VENT. CYCLES	NORMAL BEATS: OCCURRENCE	EXTRASYSTOLES: OCCURRENCE	COUPLINGS	AVERAGE CYCLE (NORMAL RHYTHM)	AVERAGE CYCLE (PARA-RHYTHM)
57	132	132		7		
58	90	222			90	139
59	56		278	*56*		
60	118	118		21		
61	92	210			92	139
62	68		278	*68*		

same as, or to have a very close anatomical relation to, that active in records made fifteen months before. The rate of discharge of stimuli bears also a close relation to the para-rhythm of the earlier record, the cycles in each varying between 130 and 150 × 0.01 second.

During the period of tachycardia following the exercise, the normal rhythm cycles measure 53 × 0.01 second. This value is sufficiently close to the relative refractory period calculated from the record to explain the absence of extrasystoles in that part of the film. Some reduction in the refractory period occurs with tachycardia, but we do not know how far this is operative in diseased or damaged heart muscle. The peculiar T-wave changes described above suggest that the recovery process in this heart was abnormal after exercise. The first isolated extrasystole, which is of similar form to the others, occurred when the normal cycles measured 88 × 0.01 second, but no others appeared for about a minute, extrasystoles finally appearing suddenly and in numbers with normal cycles of 85 × 0.01 second, and continuing to the end of the record.

SUMMARY

The case is reported of a man, aged fifty-nine years, whose electrocardiogram, taken one month after a coronary thrombosis, shewed numerous ventricular extrasystoles. The analysis of a long film record, which is given in detail in the text, shewed that these did not occur haphazardly but appeared to obey a rhythm independent of the sinus rhythm. If such an independent ectopic rhythm is postulated, all stimuli falling outwith the period during which the ventricles are refractory are effective in producing ventricular responses (extrasystoles). The case fulfills the criteria of a parasystole with simple interference dissociation. Additional evidence is afforded by the occurence of many combination complexes, intermediate in form between the normal complexes and the pure extrasystolic complexes, and due to simultaneous stimulation of the ventricle by supraventricular and ectopic stimuli.

A record from the same patient made fifteen months later shewed extrasystoles of similar form and distribution, and an analysis of a

long film record demonstrated the persistence of a parasystolic rhythm as in the original record. The extrasystoles on this occasion, however, were not present at rest, but appeared only when the tachycardia, induced by exercise, was subsiding. The probability of some abnormality in the recovery process of this heart is suggested by the concomitant T-wave changes which occur after exercise.

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THE HEART IN EMPHYSEMA*

W. B. Kountz, M.D., H. L. Alexander, M.D., and M. Prinzmetal, M.D.
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IT HAS been a time-honored belief that as a result of emphysema the heart sooner or later fails. The mechanism of cardiac damage seemed obvious, for the marked distention of the lungs was thought to impede the passage of blood from the right ventricle to the left auricle. This supposition had experimental support in that the older anatomists described narrowing and destruction of pulmonary capillaries which enter into the structure of the walls of the alveoli and which necessarily must rupture when pulmonary distention becomes sufficiently great to tear lung tissue. As a result, it has been argued that an excess load is placed upon the right ventricle in its effort to force blood through the obstructed capillary bed. This, in turn, would lead to dilatation and hypertrophy of the right ventricle, and finally to heart failure. Clinically this seemed to be true, for not only were obvious signs of cardiac decompensation found commonly in elderly individuals with senile emphysema, but dyspnea, cyanosis, and dependent edema were noted frequently in younger persons with pronounced emphysema. Some investigators have believed that all patients with emphysema die of right heart failure.

This study concerns true emphysema such as follows asthma and other obstructive lesions of the bronchi. Recently it has been shown[1] that so-called "senile emphysema" is not a pulmonary disorder at all but a degenerative process in the vertebrae which leads to "barreling" of the chest. Hence, any cardiac manifestations in these cases are independent of pulmonary findings.

Recent investigations have thrown some doubt as to whether the lung distention of emphysema offers an effective obstruction to the flow of blood through the lungs.

Kretz[2] studied the effect of emphysema, experimentally, on the right heart of dogs. He found it difficult to obtain true values of vascular pressures within the closed thorax because of the ever changing intrathoracic pressure which is distributed evenly upon all the thoracic viscera. He concluded, however, that sufficient evidence had not been presented to warrant the assumption that emphysema alone causes hypertrophy of the right heart.

Lichtheim[3] attacked the problem by tying off areas of lung tissue and found that a very considerable amount of lung had to be obstructed before a rise in pressure in the pulmonary artery could be recorded.

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Kountz, Pearson, and Koenig[4] measured the circulation time through the lungs by injecting a dye into the right heart of dogs in which emphysema had been induced. They recorded the time it took for the dye to appear in a peripheral artery and found no delay over normal dogs. Evidently there was no obstruction to the flow of blood through emphysematous lungs.

Blumgart and Weiss,[5] by injecting a radio-active substance into the vein of one arm and measuring the time it took to detect emanations in the other arm, found that only in far advanced cases of emphysema was there retardation in the rate of blood flow through the lungs.

Heinbecker[6] perfused the pulmonary artery and measured the rate of flow in relation to lung distention. It could thereby be shown that when the lungs were moderately distended the flow was increased due to straightening of capillaries and the opening of new ones, but when distended to a greater extent the flow was diminished.

From the above data it may be inferred that in obstructive emphysema the enlarged lungs do not materially affect the flow of blood from the right to the left heart, unless the process is far advanced, when some retardation may occur.

From the clinical standpoint, dyspnea, cyanosis, lowered vital capacity, and elevated venous pressure are all cardinal signs of both extensive emphysema and of cardiac failure. Moreover, dependent edema may be due to either condition. The mechanism of its occurrence is not certain, but two factors, namely, anoxemia and high capillary pressure, which, according to Landis,[7] are conducive to accumulation of fluid in the tissues, are present in emphysema as well as in cardiac failure. In emphysema the anoxemia is due directly to faulty O_2 exchange between the inspired air and the blood. The elevated venous pressure has been found to depend on the rise in intrapleural pressure which influences the amount of venous blood that enters the thorax. In some cases in which edema has been observed, post-mortem examination showed greatly distended lungs and normal hearts.

It becomes, then, very difficult to recognize from clinical signs and symptoms early cardiac decompensation in the presence of obstructive emphysema. Electrocardiograms and orthodiagrams are also misleading because the heart, pulled downward by the low diaphragm, is distorted.

In view of these observations, considerable doubt arose concerning the involvement of the heart in emphysema. This was strengthened by comparative studies of series of cases wherein it was shown that patients with obstructive emphysema in whom signs usually evident in cardiac failure, as dyspnea and edema, were present, lived much longer than those with known cardiac decompensation. The post-mortem findings of normal hearts or those smaller than normal, in cases in which emphysema

TABLE I

HUMAN HEARTS

CASE NO.	BODY WEIGHT IN KG.	APPEARANCE OF HEART	HEART WEIGHT IN GM.	RATIO OF VENT. WT. TO BODY WEIGHT	VENT. WEIGHT IN GM.	RIGHT VENT. WEIGHT IN GM.	LEFT VENT. WEIGHT IN GM.	RATIO OF RT. VENT. WT. TO LT. VENT. WT.	DURATION OF SYMPTOMS (YEARS)
1	57	Normal	260	0.00225	128	34.1	74.0	2.18	2
2	52	Normal	228	0.00271	147	44.0	87.0	1.98	10
3	62	Normal	220	0.00224	139	43.2	73.0	1.70	24
4	56	Normal	270	0.00260	145	52.0	78.0	1.50	2
5	60	Normal	325	0.00245	147	64.3	89.6	1.40	27
6	48	Normal	215	0.00260	125	38.0	52.4	1.38	3
7	50	Normal	206	0.00230	115	41.1	56.5	1.38	21
Averages	55		246.3	0.00245	135.1	45.2	72.9	1.65	14.5
8	–	Rt. vent. dil., lt. vent. hyp.	315	0.00286	166	62.4	90.3	1.45	26
9	58	Rt. vent. dil., lt. vent. hyp.	375	0.00304	177	65.0	87.4	1.34	14
10	60	Rt. vent. dil., lt. vent. hyp.	325	0.00301	181	70.1	73.6	1.05	17
11	–	Rt. vent. dil., lt. vent. hyp.	350	—	149	66.0	68.0	1.03	37
12	62	Rt. vent. dil., lt. vent. hyp.	425	0.00371	230	80.0	138.0	1.73	6
13	55	Rt. vent. dil., lt. vent. hyp.	355	0.00355	195	71.0	103.5	1.47	32
14	–	Rt. vent. dil., lt. vent. hyp.	360	—	170	68.2	98.6	1.45	2
15	58	Rt. vent. dil., lt. vent. hyp.	370	0.00343	199	71.0	101.0	1.42	25
16	58	Rt. vent. dil., lt. vent. hyp.	450	0.00345	200	77.6	97.3	1.26	21
17	–	Rt. vent. dil., lt. vent. hyp.	400	—	199	80.8	96.9	1.20	?
Averages	58.5		372.5	0.00329	186.6	71.2	95.4	1.34	22.2
Normal controls (12) averages (Herrmann and Wilson) 50.3			254	0.00294	146	45.8	78.6	1.73	

and the signs of cardiac failure had been present, contributed to the impression that in most cases of emphysema the heart in some way is spared. One recognized exception was the curious generalized cardiac enlargement, which has been observed from time to time in typical obstructive emphysema. In these instances damage to the heart was manifested by moisture at the lung bases, pronounced irregularities, and improvement under digitalis.

It appeared that clinical methods were not sufficiently accurate to give a clear picture of the effect of emphysema on the heart, and postmortem reports were not very revealing since in but few cases was particular attention paid to the heart. There was no series in which measurements by weight had been made.

EXPERIMENTAL

During the past several years, we have had the opportunity of studying the hearts of seventeen autopsied cases of emphysema. In none were valvular defects present, but in a few, especially older patients, there was some degree of fibrosis in the myocardium. In seven cases the hearts appeared normal, or were distinctly small. In ten cases there was evident enlargement. In these instances a dilatation of the right ventricle was constant, and obvious thickening of the right as well as of the left ventricular wall was seen in most instances. To reduce these observations to terms of measurements, the following weights and ratios were determined: body weight, heart weight, ventricular weight, ratio of ventricular weight to body weight, right ventricular weight, left ventricular weight, and the ratio between the right and left ventricular weights. These findings were compared with similar observations on twelve normal controls made by Herrmann and Wilson,[8] whose method of sectioning the heart was used.

The results are recorded in Tables I and I A and arranged so that the normal and the abnormal hearts are placed in separate groups. In each

TABLE I A

AVERAGE VALUES—HUMAN HEARTS

	NORMAL (7)	NORMAL CONTROLS (12) (HERRMANN AND WILSON)	RT. VENT. DIL. LT. VENT. HYP. (10)
Heart weight (grams)	246.3	(254)	372.5
Ventricular weight (grams)	135.1	(146)	186.6
Ratio of ventricular weight to body weight	0.00245	(0.00294)	0.00329
Right ventricular weight (grams)	45.2	(45.8)	78.6
Left ventricular weight (grams)	72.9	(78.6)	95.4
Ratio of right ventricular weight to left ventricular weight (grams)	1.65	(1.73)	1.34
Duration of symptoms (years)	14.5		22.2

TABLE II

AVERAGE WEIGHTS OF DRIED LUNGS—10 DOGS
(8.5 KG. TO 16 KG.)

	5 LARGE GM.	5 SMALL GM.	AVERAGE GM.	PERCENTAGE OF TOTAL LUNG WEIGHT
Right lung	15	10	12.5	55
Left lung	12	9	10.5	45
Right lower lobe	6	4.5	5.25	23
Right middle lobe	2.5	2	2.25	10
Right accessory lobe	2.5	1.5	2	8
Right upper lobe	4	2	3	13
Left lower lobe	6.5	5	5.75	25
Left middle lobe } Left upper lobe }	5.5	4.5	5	21

instance, hearts that appeared normal or enlarged on inspection proved to be so on measurement. The sole relation of the two groups to clinical

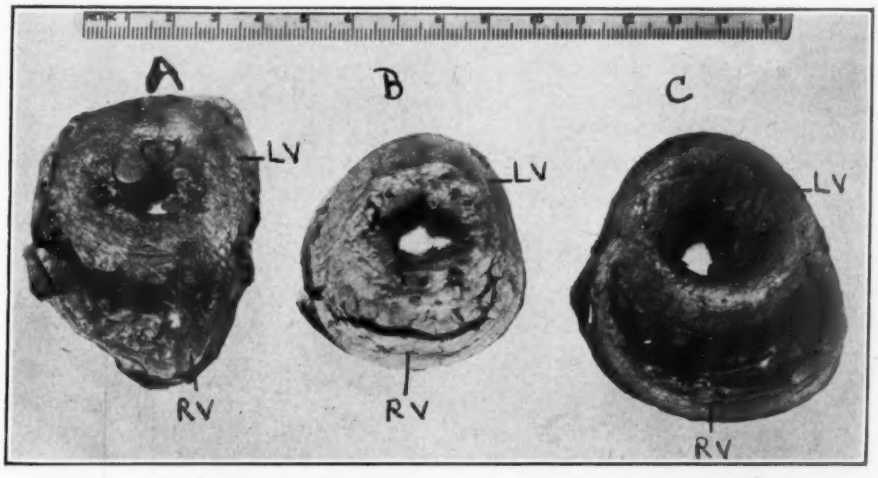

Fig. 1.—Cross-sections of hearts (*A* and *C*) from dogs with experimental emphysema. Compare with a heart (*B*) from a normal dog of approximately the same weight.

A and *C*, marked dilatation and hypertrophy of the right ventricle and hypertrophy of the left ventricle. *B*, normal heart. *RV*, right ventricle. *LV*, left ventricle.

data was that the average duration of symptoms in the series with hypertrophy was somewhat longer, although there are comparable individual cases in this regard in both groups. It was of interest that, in every instance in which right ventricular dilatation occurred, there was left ventricular hypertrophy. The reason for the latter finding is obscure.

To secure more information on the participation of the heart in emphysema, the process was studied in dogs. Advantage was taken of the observation of Adams,[10] who produced atelectasis in dogs by painting the bronchi with silver nitrate. He noted a marked compensatory emphysema in the unaffected lobes which enlarged to fill the dead space. Although the mechanism of the production of emphysema under these

TABLE III

DOG HEARTS

DOG	APPEARANCE OF HEART AT AUTOPSY	APPROX. % OF LUNG DEST.	DURATION OF EMPH. IN MO.	RATIO OF HT. WT. TO BODY WT.	RATIO OF RT. VENT. WT. TO BODY WT.	RATIO OF LT. VENT. WT. TO BODY WT.	RATIO OF RT. VENT. WT. TO LT. VENT. WT.	% O_2 SAT. OF ARTERIAL BLOOD
488	Normal	45	15	0.0087	0.0023	0.0040	1.75	94
455	Normal	55	15	0.0089	0.0026	0.0042	1.62	93
155	Normal	45	19	0.0082	0.0026	0.0041	1.54	–
154	Normal	45	41	0.0074	0.0029	0.0035	1.21	–
151	Normal	45	20	0.0068	0.0024	0.0034	1.45	94
411	Normal	55	29	0.0085	0.0031	0.0041	1.33	–
488*	Normal	58	52	0.0088	0.0026	0.0036	1.25	–
486*	Normal	55	52	0.0087	0.0031	0.0035	1.14	–
Averages		50.4	30	0.00825	0.0027	0.0038	1.410	
410†	Rt. vent. dil. and hyp., lt. vent. hyp.	68	19	0.0098	0.0031	0.0040	1.32	–
152†	Rt. vent. dil. and hyp., lt. vent. hyp.	68	23	0.0090	0.0035	0.0041	1.16	–
403†	Rt. vent. dil. and hyp., lt. vent. hyp.	58	11	0.0091	0.0038	0.0047	1.24	87
400	Rt. vent. dil. and hyp., lt. vent. hyp.	80	9	0.0099	0.0038	0.0046	1.22	72
481	Rt. vent. dil. and hyp., lt. vent. hyp.	68	12	0.0130	0.0046	0.0062	1.35	90
416	Rt. vent. dil. and hyp., lt. vent. hyp.	68	26	0.0100	0.0040	0.0046	1.16	–
412	Rt. vent. dil. and hyp., lt. vent. hyp.	76	26	0.0095	0.0035	0.0042	1.21	87
409	Rt. vent. dil. and hyp., lt. vent. hyp.	68	40	0.0095	0.0032	0.0044	1.36	92
406	Rt. vent. dil. and hyp., lt. vent. hyp.	76	34	0.0097	0.0032	0.0045	1.40	60
479	Rt. vent. dil. and hyp., lt. vent. hyp.	68	20	0.0099	0.0040	0.0050	1.23	94
405	Rt. vent. dil. and hyp., lt. vent. hyp.	76	21	0.0094	0.0039	0.0040	1.03	74
Averages		70.4	21.9	0.0099	0.00369	0.00457	1.244	
Normal controls (200 dogs) (Herrmann) Averages				0.00798	0.00265	0.00369	1.393	

*Questionable right ventricular dilatation.
†Right ventricular dilatation prominent.

circumstances differs from the cases in man recorded above which resulted from bronchial obstruction, nevertheless the alveolar and vascular lesions in the lungs were identical in each. In order to produce considerable pulmonary distention, large amounts of lung, as much as 80 per cent, were destroyed, one lobe at a time. These were first made atelectatic and then removed surgically by successive operations. It appears that the amount of lung destruction has a definite bearing on the production of cardiac lesions, so that a method was worked out to estimate the proportion of the lung removed. This was done by weighing separately the dried lungs and the separate lobes of ten normal dogs (large and small) and estimating the percentage of each to the total lung weight (Table II).

Nineteen dogs survived the operations. The duration of emphysema was arbitrarily estimated from the date of the last operation until postmortem examination. These periods varied from nine months to fifty-two months. When arranged into two groups, it is seen that eight hearts appeared essentially normal on inspection and eleven were pathological. Of the latter, right ventricular dilatation was prominent in all. The others showed some hypertrophy of the right and left ventricles. As with the human hearts, measurements confirmed the appearance of the organ, and again in each instance in which the heart was abnormal, both the right and left ventricles were involved. The measurements were compared with averages of the large series of controls established by Herrmann.[9] It is recognized, however, that in that series there were wide variations and that some of the figures recorded here as pathological are duplicated in normal animals. These, however, are not sufficiently numerous to affect the averages seriously.

TABLE III A

AVERAGE VALUES—DOG HEARTS

	NORMAL (8)	NORMAL CONTROLS (200) (HERRMANN)	RT. VENT. DIL. LT. VENT. HYP. (11)
Ratio of heart weight to body weight	0.00825	(0.00798)	0.00990
Ratio of right ventricular weight to body weight	0.00270	(0.00265)	0.00369
Ratio of left ventricular weight to body weight	0.00380	(0.00369)	0.00457
Ratio of right ventricular weight to left ventricular weight	1.410	(1.393)	1.244
Amount of lung destroyed—percentage	50.4		70.4
Duration of emphysema (months)	30		21.9

DISCUSSION

The finding of cardiac damage in most of the cases studied refutes the more recent impressions that in emphysema the heart is usually not affected. How much the lesions observed contribute to clinical symptoms is debatable.

Of particular interest is the left ventricular hypertrophy which, in the absence of peripheral hypertension, cardiac infarct, myocardial degeneration, or other conditions associated with enlargement of the heart, is difficult to account for. Hoover was, perhaps, the first to discuss this problem. He suggested that, because of the faulty exchange of oxygen through emphysematous lungs, there may be a partial asphyxia of the heart muscle which would lead to increased effort and generalized hypertrophy. In this connection, it is interesting that Vacek[11] was able to produce a generalized cardiac hypertrophy in mice exposed to various degrees of low oxygen tensions. Stronghold[12] induced partial asphyxia in animals and found that a reduction of oxygen in the inspired air resulted in an increase of both the diastolic volume and systolic discharge, thus increasing the work of the heart.

Hoover's theory, namely, that generalized cardiac hypertrophy is due to asphyxia, is at present under investigation and will be the subject of a further communication. Kountz and Gruber[13] produced acute cardiac asphyxia in dogs by the injection of pressor substances, as well as by general asphyxia, and obtained a typical elevation of the S-T segment of the electrocardiogram. We have seen no such curves in patients with advanced emphysema, nor in emphysematous dogs with large hearts whose arterial oxygen content was greatly reduced by exercise. It is possible that changes in the electrocardiogram noted above are dependent upon the suddenness of the asphyxia of the heart muscle.

Geizel[14] explained the generalized ventricular hypertrophy of emphysema as due to increased abdominal pressure caused by the forced descent of the diaphragm. A resistance to a large part of the peripheral blood flow would thereby be offered and the heart respond by more forceful contraction of the left ventricle. He believed that the elevated intra-abdominal pressure likewise would hasten the return flow of venous blood through the inferior vena cava to the right heart, whose intake would thus no longer be regulated by the intrapleural pressure. Geizel concluded, therefore, that both chambers of the heart would be at a disadvantage in emphysema and hypertrophy of each would occur. That this explanation is not entirely tenable is indicated by data presented below which show that when emphysema is sufficiently advanced to produce symptoms, there is probably a diminution in the amount of blood in the right auricle rather than an increase.

The left ventricular hypertrophy remains as yet unexplained. The cause of the right ventricular dilatation also is not certain. The assumption that this is due merely to the resistance offered by the reduced capillary bed in the lungs is not borne out by the experiments cited at the beginning of this paper, wherein only with very advanced emphysema does such obstruction seem to occur. Dilatation of the right ventricle has been observed in patients in whom emphysema was not of that degree.

It is entirely possible that this lesion occurs in the earlier stages of emphysema. The suggestion is based on the fact that as the diaphragm descends with the enlarging lungs the intrapleural pressure becomes more negative and the blood flow to the right heart increased. Overloading may take place at this time. Once the diaphragm is pushed down to its position of contraction and the excursion of the thorax limited by its barreling, the intrapleural pressure promptly rises, and the blood flow into the thorax becomes impeded.

This sequence of events in emphysema has been indicated by the induction of pulmonary distention in animals. In dogs, partial tracheal obstruction produced by a ball valve which offers resistance to expiration leads to marked emphysema. As the lungs distend, the intrapleural pressure falls and likewise the peripheral venous pressure. When the lungs are fully distended, the intrapleural pressure rises to be followed in a few days by rise in the venous pressure, which points to a retardation of blood returning to the heart.[15] This interpretation has been confirmed by the experiments of Kountz, Pearson, and Koenig, who measured the circulation rate in dogs with emphysema and found a delay in blood flow from the periphery to the right auricle and none from the right auricle to the left ventricle. Alexander[16] and his associates studied the problem in guinea pigs with anaphylactic shock during the period of lung distention. Here again, as the lungs enlarged, the intrapleural and peripheral venous pressures fell, whereas the effective pressure in the right auricle *rose*. When the lungs were fully distended, the reverse abruptly occurred—a rise in intrapleural and venous pressures and a *fall* of pressure in the right auricle, which appeared to be due to a diminished amount of blood entering the heart.

Obstruction to the flow of blood from the right side of the heart to the left brought about by diminution of the capillary bed in emphysema may contribute to the right ventricular dilatation, but only in the late stages of the disease.

As yet no explanation is available to account for the fact that in a considerable proportion of cases of emphysema, both clinical and experimental, the hearts were normal, in contrast to similar cases with cardiac damage.

SUMMARY

From these observations it appears (1) that the heart is affected in the majority of patients with emphysema; (2) that the lesion, cardiac hypertrophy, with dilatation of the right ventricle when advanced, may produce symptoms, but probably has no clinical reflection in its earlier stages; (3) that the cause of the left ventricular hypertrophy remains, as yet, undetermined; (4) that there is experimental evidence which indicates that the right ventricular dilatation and hypertrophy occur chiefly in the earlier stage of emphysema, when the lungs are in the process of distention, rather than later as generally believed.

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A CLINICAL STUDY OF THE ELECTROCARDIOGRAM AND OF THE PHASES OF CARDIAC SYSTOLE IN PELLAGRA*

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PELLAGRA, long regarded as a serious and frequently fatal disease, now may be cured in a high percentage of cases by means of adequate diet and large supplements of yeast or liver extract.[1-4]

In his study of pellagra patients, Spies noted tachycardia and faint heart sounds and concluded that pellagra affects the circulatory system. Stimulated by his observations I undertook this study of pellagra. In Spies' series of 125 cases (37 per cent of which were recurrences), he has a recovery record of 94 per cent. The 6 per cent of fatal cases, in all but one instance, showed the presence of complications (from post-mortem studies) as at least contributory causes of death. Other authors have reported cases of sudden death in patients who were apparently convalescent.

The 38 patients of this study were all under the supervision of Dr. Tom D. Spies on the medical service at Lakeside Hospital, and all were hospitalized. All of the 38 patients presented the typical picture of pellagra with cutaneous, gastrointestinal, and neurological symptoms of varying degree. Thirty-seven of the patients had had an inadequate diet associated with chronic alcoholism. In one case, in which a youth of fifteen years did not take alcoholic beverages, pellagra followed partial starvation. The patients varied in age from fifteen to seventy-six years, and the average age was 40.8 years. There were 21 males (15 white and 6 colored) and 17 females (1 white and 16 colored.) In view of the predominance of the middle-aged patients, a careful search was made for the presence of other possible factors in producing cardiovascular disease. In none of the cases were drugs administered which might have affected the electrocardiogram. (Further reference to these factors is made later in the paper.)

Porter[5] recently reported that in 20 endemic† pellagrins it was found that the hearts were of the asthenic type, that there was a moderate degree of sinus tachycardia even after the clinical symptoms had disappeared, and that the electrocardiograms taken biweekly throughout the duration of clinical symptoms were, without exception, normal. Hypertension was not noted in any patient. Porter concluded from his study

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†Only one in this series is endemic. It may be concluded that these alcoholic patients may belong to the group having tendency to develop hypertension.

that pellagra occurs in patients with a hypoplastic cardiovascular apparatus of constitutional origin. In the 38 cases which I am reporting, the systolic blood pressure was above 150 mm. in 5 cases (13.2 per cent), between 130 mm. and 150 mm. in 24 cases (63.1 per cent), and below 130 mm. in 9 cases (23.6 per cent).

Campbell and Allison[6] reported eight cases of toxic polyneuritis of undetermined origin with electrocardiographic observations in three cases. These patients, in addition to the mild neuritic symptoms, had palpitation, vomiting, dyspnea on exertion, and swelling of the feet and legs. The electrocardiograms were characterized by inversion of T_1 in one case and of T_2 and T_3 in two cases. Upon recovery, the negative T-wave became positive. While these cases cannot be classified either as beriberi or pellagra, it is possible that a food deficiency was the etiological factor.

The "beriberi heart" has been studied by several investigators.[7-11] The electrocardiogram was normal in approximately two-thirds of the cases. In one-third of the cases low voltage, notching of the QRS in all leads, high T-waves, changing sign of T with recovery, and changes in

TABLE I

ELECTROCARDIOGRAPHIC FINDINGS

	NO. CASES	PERCENTAGE
Normal records	19	50.0
Abnormal records	19	50.0
Abnormal records without complications	14	36.8
Sinus tachycardia (90 or over)	26	68.4
Auricular fibrillation (mitral stenosis)	1	2.6
Ventricular premature beats	2	5.2
Normal voltage	37	97.4
Low voltage of QRS (below 5 mm.)	1	2.6
Large T (1, 2, or 3)	2	5.3
Pardee S-T	8 (a)	20.5
Unquestioned	(5)	
Lead I)3		
Lead II)1		
Lead III) 4		
Inverted S-T	4	11.0
Everted S-T (b)		
Negative T_1) 4		
T_2) 2	10	26.3
T_3) 4 (c)	6	16.0 (unquestioned)
Abnormalities of Lead IV (apex—left leg)	12 (d)	36.4 (e)
Low voltage	3	
Monophasic S-T	2	
Upright T	10	
M complex (QRS)	1	

(a) Includes one case of aortic insufficiency and two cases of hypertension.

(b) Includes one case of hypertension and one case of mitral stenosis.

(c) Includes two cases of hypertension, one case of acute rheumatic fever, and one case of syphilitic aortic regurgitation.

(d) Includes one case of hypertension and one case of aortic insufficiency.

(e) Lead IV taken in thirty-three cases.

the P-R interval (variable) were present. These changes, while not diagnostic, tend to support the clinical findings that the heart is affected in beriberi.

Electrocardiographic Study.—Electrocardiograms were taken in all cases during the relapse of the disease and in eighteen of the cases during convalescence as well. The records were normal* in nineteen of the cases (50 per cent). In Table I are collected all of the data of the records. Careful examination of the patients revealed a number with evidence of cardiovascular disease, and reference to these findings is made in the table. The chief changes were sinus tachycardia, S-T changes similar to those described by Pardee (Fig. 1) in myocardial fibrosis sec-

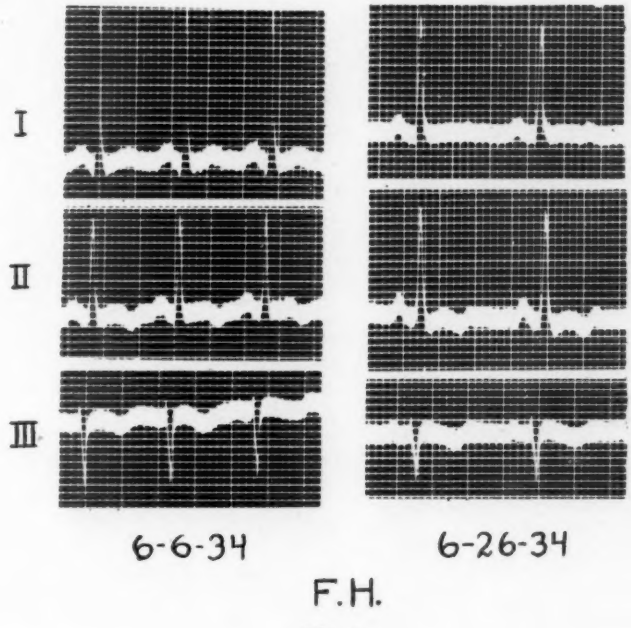

Fig. 1.

ondary to coronary disease, and inversion of T in Leads I or II or both (Fig. 2). In some instances these changes persisted, and in other cases with recovery there was a return to normal (Fig. 3). *In no case was digitalis or any drug known to affect the electrocardiogram administered.* The sinus tachycardia frequently persisted during the convalescence, and in some instances increased. Large T-waves were occasionally seen. In three cases the S-T portions of the curves were monophasic in type (Fig. 3a). The P-R interval in the thirty-eight cases varied from 0.12 to 0.21 second during the attack. In eighteen cases after convalescence was established, the P-R interval varied somewhat but not consistently. The

*Sinus tachycardia was not classified as an abnormal finding and cases were included in the 50 per cent group unless definite evidence of other abnormality was found.

QRS interval during the attack varied from 0.05 to 0.12 second and was approximately the same during the convalescence in the eighteen cases in which records were taken.

Lead IV (apex—left leg) was recorded in 33 of the 38 cases. In 12 instances this derivation was abnormal (36.4 per cent of the 33 cases). The abnormal findings are tabulated in Table I. In none of the cases with abnormal conventional records was Lead IV normal. In 4 cases Lead IV was abnormal with normal conventional leads. Progressive

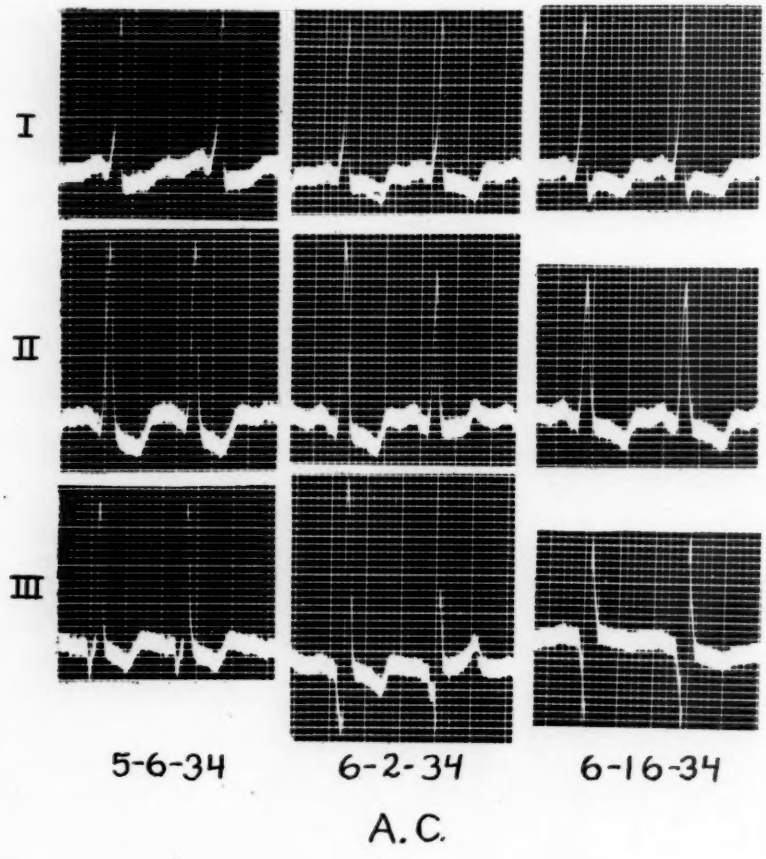

Fig. 2.

changes in Lead IV occurred in 3 cases without alterations in the standard leads, when taken during the activity of pellagra and during convalescence. In Fig. 4 are illustrated the various types of abnormal Lead IV.

The *M* QRS complex was present in Lead IV in 1 case (Fig. 4*a*); low voltage of the entire QRS complex was present in 3 cases (Fig. 4*b*), an upright T was present in 10 instances (Fig. 4*c*), and S-T was monophasic in 2 cases (Fig. 4*d*).

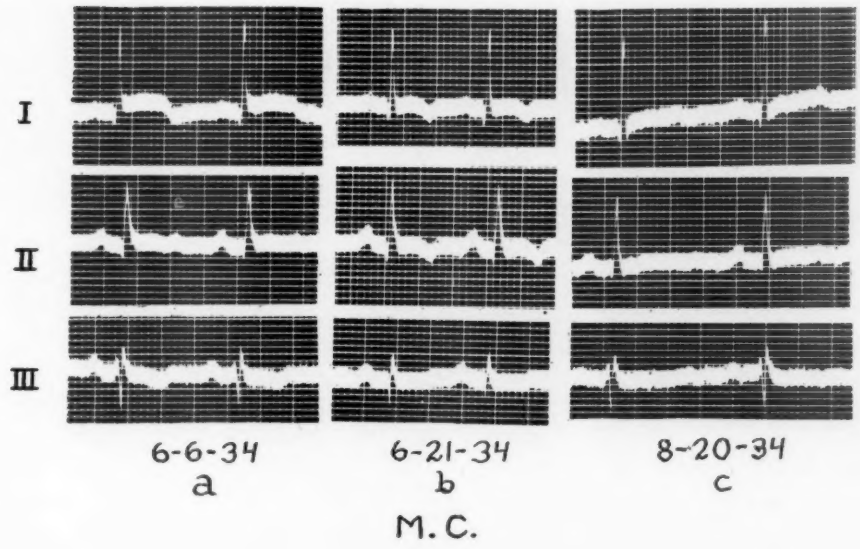

Fig. 3.

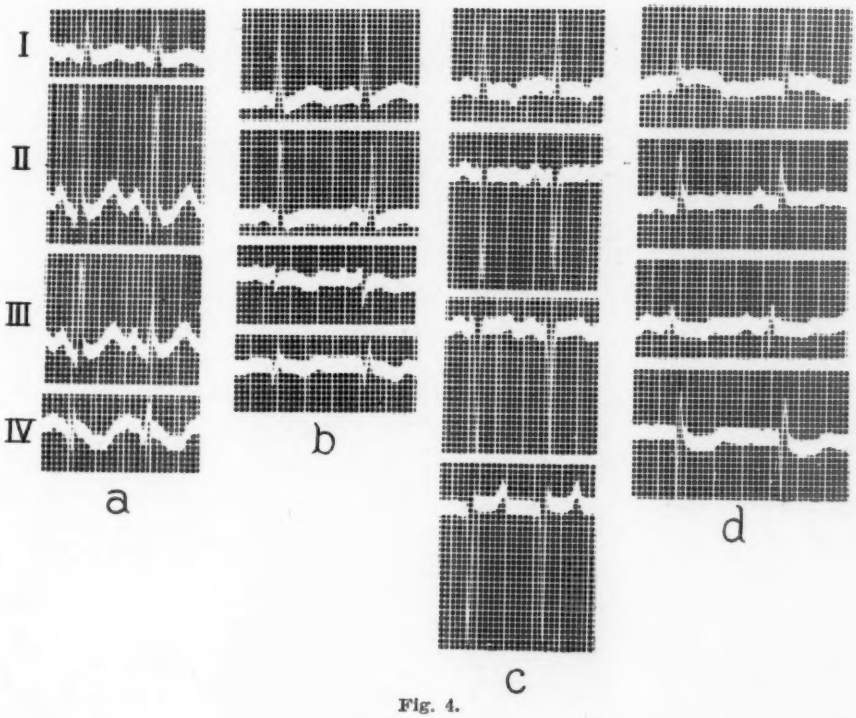

Fig. 4.

In Table II are the measurements of the P-R and QRS intervals in 18 cases during the acute stage of the disease and after convalescence was

TABLE II

MEASUREMENTS OF P-R AND QRS INTERVALS DURING ATTACK AND DURING CONVALESCENCE

PATIENT	P-R		QRS	
	ATTACK	CONVAL.	ATTACK	CONVAL.
M. C.	0.19	0.17	0.09	0.07
G. B.	0.14	0.14	0.08	0.08
A. C.	0.14	0.14	0.12	0.11
P. G.	0.14	0.13	0.07	0.07
W. H.	0.19	0.19	0.10	0.07
R. L.	0.14	0.18	0.07	0.06
A. L.	0.14	0.13	0.07	0.07
B. L.	0.14	0.14	0.09	0.09
L. S.	0.16	0.16	0.05	0.06
C. K.	0.21	0.22	0.06	0.06
G. P.	0.12	0.14	0.07	0.06
C. C.	0.16	0.16	0.06	0.07
E. H.	0.14	0.14	0.07	0.05
A. C.	0.14	0.16	0.08	0.08
A. S.	0.11	0.14	0.07	0.08
W. C.	0.18	0.14	0.09	0.07
E. F.	a. f.	0.20	0.07	0.09
M. B.	0.15	0.15	0.09	0.07

TABLE III

ELECTRICAL SYSTOLE

PATIENT	PELLAGRA SEVERE			CONVALESCENT		
	CYCLE SEC.	RATE	Q-T	CYCLE SEC.	RATE	Q-T
M. C.	0.78	77	0.39	0.53	113	0.31
G. B.	0.84	71	0.38	0.53	113	0.29
A. C.	0.62	97	0.37	0.55	109	0.36
P. G.	0.75	80	0.42	0.57	105	0.36
W. H.	0.88	68	0.46	0.91	66	0.43
R. L.	0.86	70	0.38	0.79	76	0.38
A. L.	0.79	76	0.37	0.57	105	0.26
B. L.	0.49	123	0.34	0.49	123	0.34
L. S.	0.70	86	0.32	0.75	80	0.34
C. K.	1.03	58	0.41	1.05	57	0.40
G. P.	0.70	86	0.35	0.64	81	0.35
N. K.	0.56	107	0.33	0.77	78	0.39
R. R.	0.47	128	0.30	0.45	133	0.31
E. S.	0.80	75	0.40	0.57	105	0.34
A. S.	0.77	78	0.37	0.60	100	0.34
F. B.	0.53	113	0.34	0.55	109	0.35
A. C.	0.76	79	0.38	0.60	100	0.32
E. F.	0.57	105	0.36	0.67	82	0.37
F. H.	0.48	125	0.27	0.65	92	0.32
E. H.	0.53	113	0.34	0.48	125	0.26
C. H.	0.69	81	0.38	0.74	70	0.39

well established. The Q-T interval was measured in three consecutive cycles in each record and the averages recorded on the graphs (Figs. 5 and 6.) The normal controls* were obtained from measurements of

*From the same age group.

electrocardiograms of young normal adults by Dr. R. A. Shipley and Dr. William R. Hallaran.[12] The normal subjects are recorded as solid dots and the pellagrins as circles. The diagonal lines were drawn to show the limits of normal. In all instances, systole (Q-T abscissae) was plotted against cycle length (ordinates). Both graphs show that there

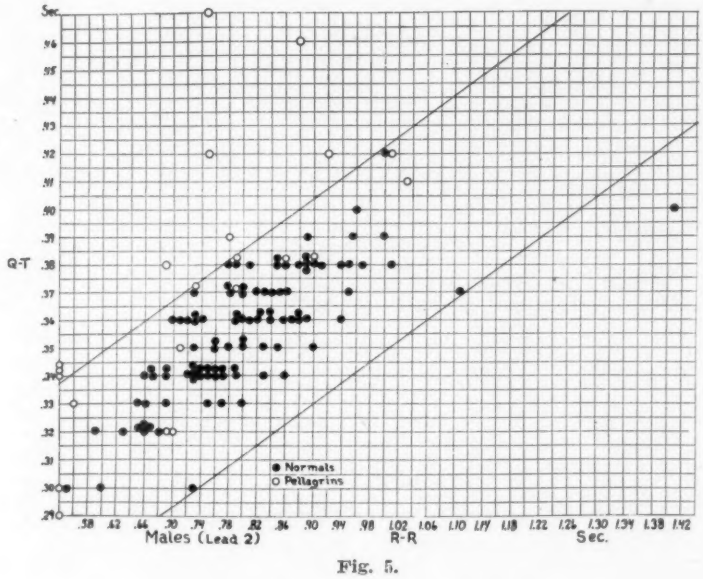

Fig. 5.

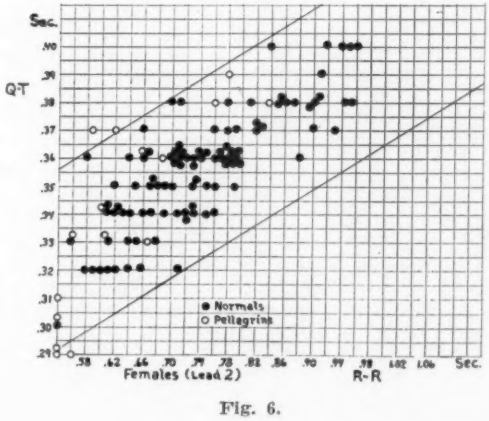

Fig. 6.

is a tendency for systole to be prolonged, especially with slower rates. Observations made after recovery show that in many instances Q-T is shortened. This change was found to be true in both male and female patients. Table III is a complete record of these observations. When the average Q-T was determined by the formula of Cheer and Dieuaide[13] $Q\text{-}T = K \sqrt{C}$ (Q-T and C in seconds and K a constant) it was found that

the average value of K for the male pellagrins was 0.437 (normal K = 0.397[y]) and for the females 0.430 (normal K = 0.415[z]).*

In eleven instances, electrical systole was shortened during recovery; it was unchanged in three instances and was lengthened in seven cases.† Because of the frequent variation in heart rate, these figures cannot be studied without taking the cycle length into consideration. Figure 7 was constructed by plotting the duration of Q-T of the individual observations against cycle length (R-R). The solid dots represent Q-T before treatment and the circles after treatment in twenty-one cases.

Alcoholism and the Electrocardiogram.—Nine patients suffering from alcoholism but without evidence of pellagra were studied electrocardiographically. In all cases the records were normal. The P-R, the QRS, and the Q-T intervals were measured (Table IV), and in all instances these intervals were found to be within normal limits. In six of these cases, records were taken after all signs of alcoholism had disappeared and when the patients were ready for discharge from the hospital. The Q-T interval was unchanged in all of the cases.

TABLE IV

MEASUREMENTS OF P-R, QRS, AND S-T IN ACUTE ALCOHOLISM WITHOUT EVIDENCE OF PELLAGRA

PATIENT	HEART RATE	P-R		QRS		Q-T	
		ALCOHOLISM	CONVAL.	ALCOHOLISM	CONVAL.	ALCOHOLISM	CONVAL.
J. C.	63	0.17		0.07		0.38	
	77		0.16		0.05		0.36
A. M.	93	0.14		0.06		0.31	
E. C.	73	0.14		0.06		0.34	
	110		0.14		0.04		0.28
O. N.	96	0.14		0.04		0.32	
	102		0.14		0.06		0.32
E. S.	80	0.17		0.05		0.36	
	90		0.17		0.05		0.36
C. T.	83	0.14		0.06		0.33	
R. F.	88	0.14		0.06		0.35	
C. F.	90	0.18		0.06		0.34	
	100		0.18		0.06		0.34
J. C.	90	0.13		0.05		0.33	
	100		0.13		0.05		0.32

Other Possible Factors Causing Changes in the Electrocardiogram.—There is a possibility that metabolic factors such as low blood calcium (as in deficiency of parathyroid hormone) and changes in water balance and in the acid-base equilibrium, play a rôle. These factors are being investigated by Dr. Tom D. Spies.

*Y, normal range of K for males: 0.337 to 0.433; Z, normal range of K for females: 0.380 to 0.456 (Normal series of Shipley and Hallaran).

†The prolongation of mechanical and of electrical systole was not limited to the group with hypertension.

In summary, Q-T is frequently prolonged in pellagra, and, when the cycle length is considered, there is frequently an abbreviation during convalescence.

The Phases of Systole (Mechanical Systole).—Simultaneous records of heart sounds and the subclavian pulse were recorded photographically by the method described by Wiggers,[14] and the phases of systole

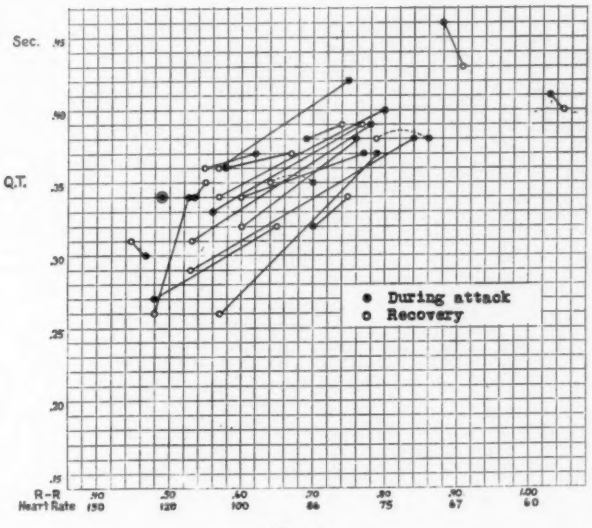

Fig. 7.

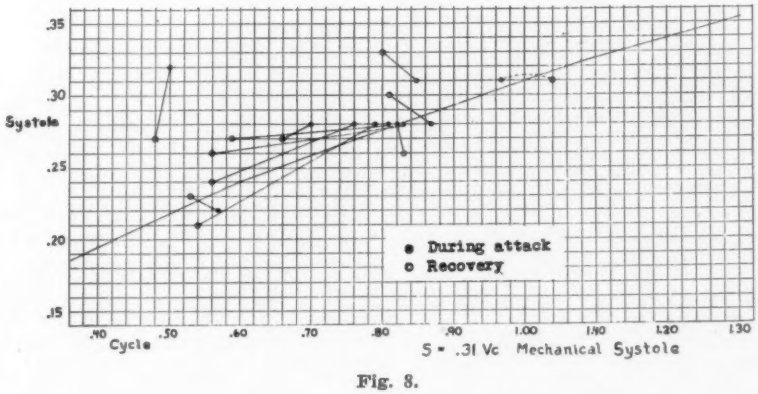

Fig. 8.

were computed by a method described by Katz and Feil.[15] In twelve patients, observations were made during the acute stage and after convalescence began. Table V is a complete summary of the figures of the isometric and ejection phases and of total systole with corresponding cycle lengths. When the recorded systole is compared with the calculated systole ($0.31\ \sqrt{C}$), it is seen that systole was prolonged in five cases and abbreviated in but one instance. During convalescence

systole was prolonged in seven cases, the same in one case, and shortened in two instances. When systole during the disease is compared with systole during convalescence and plotted against cycle length, the frequent abbreviation of systole during convalescence is made clear (Fig. 8). It may be concluded then that pellagra tends to prolong mechanical systole and that recovery frequently reduces this interval. The isometric phase varied from 0.04 to 0.09 second during the attack and from 0.05 to 0.11 second after the attack. No consistent change occurred in individual cases. The ejection phase was reduced in six cases during convalescence. The changes in the duration of systole were due to changes in ejection time.

TABLE V

MECHANICAL SYSTOLE

PATIENT	CYCLE LENGTH		RATE		ISOMETRIC PHASE		EJECTION PHASE		TOTAL SYSTOLE		$S = 0.31 \sqrt{C}$	
	ac.	con.	ac.	con.	ac.	con.	ac.	con.	ac.	con.	ac.	con.
M. C.	0.79	0.54	76	111	0.05	0.05	0.23	0.16	0.28	0.21	0.275	0.228
G. B.	0.83	0.56	72	107	0.06	0.06	0.22	0.19	0.28	0.26	0.282	0.232
A. C.	0.57	0.53	105	113	0.06	0.05	0.16	0.18	0.22	0.23	0.234	0.227
P. G.	0.76	0.56	79	107	0.04	0.06	0.24	0.18	0.28	0.24	0.271	0.232
W. H.	0.87	0.81	69	74	0.04	0.07	0.24	0.23	0.28	0.30	0.288	0.279
R. L.	0.85	0.80	71	75	0.07	0.10	0.24	0.23	0.31	0.33	0.286	0.276
A. L.	0.81	0.59	74	101	0.08	0.09	0.20	0.17	0.28	0.27	0.278	0.237
B. L.	0.50	0.48	120	125	0.08	0.11	0.15	0.16	0.32	0.27	0.219	0.215
L. S.	0.83	0.83	72	72	0.09	0.08	0.19	0.19	0.28	0.26	0.280	0.282
C. K.	0.97	1.04	62	58	0.08	0.08	0.23	0.24	0.31	0.33	0.304	0.316
G. P.	0.70	0.66	86	91	0.08	0.05	0.20	0.22	0.28	0.27	0.259	0.252
C. C.	0.69	0.74	87	81	0.05	0.10	0.20	0.23	0.25	0.33	0.257	0.267

NOTE.—Electrical and mechanical systole were not always concomitantly prolonged.

Pathological Findings.—Twelve patients dying of pellagra were studied pathologically, but only one of this group had electrocardiograms and observations on the duration of the phases of cardiac systole. The hearts were examined in all cases macroscopically and microscopically by Dr. Francis Bayless. No gross changes were noted, nor were there significant changes in the microscopic sections. The heart weights of fourteen autopsied cases are recorded in Table VI. Of the six females the heart weight was below the average normal weight in four cases and slightly increased in two instances. In both of these cases the blood pressure was within normal limits (M. M. and A. J.). Of the eight males the heart weights were increased in two instances, in both of which the blood pressure was within normal limits (J. S. and H. D.). One patient had arteriolar nephrosclerosis in addition to pellagra, but elevation of blood pressure was the only clinical evidence of the disease. The heart of this patient, a colored male of forty-five, weighed 340 gm., and the myocardium was normal both macroscopically and microscopically. There were small arteriosclerotic plaques on the intima of the large coronary vessels, but no narrowing of the lumina was present.

TABLE VI

HEART WEIGHTS IN POSTED PELLAGRINS WITH AVERAGE BLOOD PRESSURE READINGS

PATIENT	SEX	AGE IN YR.	HEART WEIGHT IN GM.	B.P.
M. M.	F.	30	370	118/ 82
A. J.	F.	30	320	100/ 76
C. W.	F.	24	230	140/ 98
P. P.	F.	26	165	80/ 60
H. P.	F.	33	205	90/ 60
C. J.	F.	27	230	126/ 88
J. S.	M.	62	440	118/ 84
R. B.	M.	36	290	135/ 90
T. G.	M.	79	300	145/105
H. D.	M.	37	420	130/115
A. G.	M.	65	300	110/ 60
M. C.	M.	45	340	170/126
H. P.	M.	52	370	144/100
A. M.	M.	45	340	184/104

Roentgenographic Findings.—In a number of cases teleroentgenograms were taken during and after the attack. The heart was usually normal (unless valve lesion or hypertension was present). There was no deviation from the normal contour of the silhouette.

DISCUSSION

Acute pellagra is frequently associated with cardiovascular symptoms: subjectively, dyspnea on effort and palpitation; and objectively, tachycardia, feeble heart sounds, and slight edema in some instances. The prolongation of electrical systole and the frequent lengthening of mechanical systole may be the expression of abnormal cardiac function. The electrocardiogram was abnormal in 36.8 per cent of thirty-eight clinical cases of pellagra without complications. This figure may be compared with the figure of Keefer[11] in beriberi (37 per cent). Pellagra and beriberi apparently affect the heart physiologically in much the same way. The cardiac manifestations in pellagra, however, are less severe. Acute alcoholism was not responsible for the electrocardiographic changes seen in the pellagrins.

SUMMARY

In this study of 38 patients with moderate to severe pellagra, electrocardiographic abnormalities in the ventricular complex occurred in 50 per cent. In 14 of these 19 patients there was no complication which might alter the electrocardiogram (36.8 per cent). The chief abnormalities were inversion of T in Leads I or II or both, Pardee type of S-T, and large T-waves. Lead IV was abnormal in 12 instances out of 33 cases in which it was recorded (36.4 per cent). Lead IV was abnormal in 4 cases with normal Leads I, II, and III. The Q-T interval and mechanical systole were prolonged in some cases. These findings

suggest that the heart is affected physiologically in pellagra. Twelve hearts (one of which was studied electrocardiographically and dynamically) examined pathologically showed no gross or microscopic abnormality. Roentgenographic changes were lacking in the cases studied.

Thus it may be concluded from these clinical, electrocardiographic, and dynamic studies that the heart is affected by pellagra.

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ELECTROCARDIOGRAMS ON 167 AVERAGE HEALTHY INFANTS AND CHILDREN*

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THE 1,276 electrocardiograms which form the basis of this study were taken on 167 healthy children, of whom 85 were boys and 82 were girls. They ranged in age from three weeks to twelve years. The majority of these (115) form a group of average healthy children of the community who are being followed from birth to maturity. They are brought in the first time during the third or fourth week of life and every month for the first three months, then at approximately three-month intervals for so long as we are able to follow them, the oldest now being over 12 years of age. The routine consists of complete physical examinations, roentgenograms of chests, sinuses, spines, wrists, heads and teeth, electrocardiograms, anthropometric measurements, basal metabolism tests, with dental checks every six months and psychometric, social, and behavior studies once each year. Careful family histories and records of the prenatal and newborn periods are obtained, and all additional departmental findings, information, and reports are subsequently added. The "Special Series" of 52 was not started at birth, but they have been referred to us for special reasons and have been followed in the same manner.

The electrocardiographic study was started five and one-half years ago. Our records represent repeated electrocardiograms on the same children for this period of time. The greatest number of records on one child is seventeen, with an average of 7.6 records on each child. The records of two of the "Birth to Maturity Series" have been dropped from this study as there was a question as to whether or not they were in average health.

RÉSUMÉ OF LITERATURE

In 1908 Funaro[1] under the direction of Nicolai and at Heubner's suggestion made the first electrocardiograms on infants and children. Only Lead I was taken on forty-five children. They found S_1 frequently deep. Heubner[2] a little later in that year also noted the deep S_1. He also called attention to the small or absent R-wave in the first lead in infants. In 1913 Hecht[3] took a group of seventy children consisting of premature infants, newborn infants, and young and older children, but all were not normal. At different periods he found

*From the Child Research Council and the University of Colorado School of Medicine, Denver, Colo.

S_1 less than R_1 in different subjects. P_1 was found split once, and R and S split more frequently especially in older children. The T-wave was small in infancy and inconstant in Lead III at all times.

In 1913 Noeggerath[4] studied a series of sixty-eight normal (?) children, taking only Leads I and II.

In 1917 Krumbhaar and Jenks[5] presented their studies on forty-two normal subjects whose ages ranged from immediately after birth to eleven years. They found that a right preponderance was present until the second or third month and by the sixth month the infant's electrocardiogram had become practically the same as that of the adult. R_2 became greater than R_3 about the sixth week, but S_1 persisted abnormally large for several months; Q-wave, prominent throughout their series, especially Q_2 and Q_3; T- wave, absent for the first week and after the first three weeks reached a "proportionate size," and largest and frequently inverted in Lead III; and the P-R interval, shorter than in the adult.

In 1920 electrocardiograms were taken by Seham[6] on 101 normal children from one hour to thirteen years of age. He found that the P-wave was higher in childhood than in the adult; Q-wave, deeper than in the adult, and added confirmatory evidence that there is a right ventricular preponderance in the first few months of life, R, generally much higher than in the adult; S_1, deeper in the first three months than in any other period of life and in other leads relatively deeper than in the adult; T, frequently absent in the first ten days of life and after that quite constant; T_1, more regular than T_2 and T_3 which was inverted in 15 per cent of the cases between six and thirteen years; and the transmission time, on the whole, shorter than in the adult.

In 1928 Brughaard and Wurnerlich's[7] studies consisted of 115 electrocardiograms on premature infants, newborn infants, and older infants. That same year Lincoln and Nicolson[8] published their study of 222 normal school children from three to twelve years of age. They established a series of normal figures for each age period, with standard deviations. They showed the possible sex and family characteristics and stressed the difference between the tracings of an adult's heart and a child's heart. They found that the P-, R- and T-waves were higher than in the adult and the transmission time shorter. The Q- and S-waves were not constant and decreased with age, this decrease being most marked in Q_3, while S_3 showed an irregular increase in depth from year to year, and T_3 was inverted in 35.5 per cent of their cases. An average of 62 per cent of the children showed a sinus arrhythmia.

In 1931 Shookhoff and Taran's[9] series of 259 normal children from six to fourteen years of age was published. P_3 was split, diphasic, or inverted in 17.6 per cent of the cases in Lead III. A widening and

a slight slurring of QRS interval in Lead III was seen in 34.8 per cent; and T_3 was inverted in 24.8 per cent of their cases.

TECHNIC AND PROCEDURE

The first twenty-two records used in this study were taken with a string galvanometer type of machine. Technical difficulties encountered in taking records of infants and younger children directed us to the beam galvanometer.* With the exception of these twenty-two early records all were taken on this machine. In several of the early records the same child had electrocardiograms taken on both machines, one record succeeding the other. It was found that both checked very well. Standard electrocardiographic methods were used throughout; namely, 1 cm. of deflection of string or beam for 1 millivolt introduced into the circuit and the three customary arms and leg leads. Outing flannel bands with pockets, moistened in warm saline solution, were used to apply the electrodes.

An endeavor was made to quiet the child, but nothing further was attempted, and conditions were similar in every way to those existing in the physician's office. The infants up to seven months of age were taken lying in a crib. From that age to three years six months in boys and three years in girls 158 records were taken in the sitting position while 325 were taken in the supine position. In the first group when the child moved too much in the lying position, he was allowed to sit up alone or in his mother's lap, rubber aprons being used to insulate the parent so that we could get a measurable record. Of those taken in the sitting position there were only seven tracings which established the high or low limits in amplitude for a given wave within one age group. This was checked by a change from the supine to sitting posture at a later date. In only one instance was there a change in that particular wave whose amplitude had previously been high or low.

These electrocardiograms were interpreted according to accepted standards. In the discussion to follow, reference will be made to adult standards which unless otherwise stated will refer to standards of the Heart Committee.[10]

With this brief introduction on technic and procedure, we present our observations on the amplitude and form of each individual wave and the intervals and rhythms encountered.

THE P-WAVE

Amplitude.—In our series higher and lower amplitudes were found than in the adult, considering the upper limit as 2.5 mm. and the lower limit as 0.5 mm. High amplitude was more marked in the girls

*Through the courtesy of the General Electric Corporation we were allowed the use of a Victor Electrocardiograph.

TABLE I

AMPLITUDE MEASUREMENTS OF THE P-, Q-, R-, S-, AND T-WAVES BY PRECEDING AND PRESENT AUTHORS

WAVES	AUTHORS	AGE	3 WK. TO 6 MO.		7-12 MO.		13-18 MO.		19-24 MO.		2-3 YR.		3-4 YR.		4-5 YR.		5-6 YR.		6-7 YR.		7-8† YR.	
		LEADS	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.
P	Krumbhaar and Jenks[5]	I mm.	0-1.5		1		1		1		2						1.5		2		2	
		II	1-2		1		1		1-2		2						2		3		2	
		III	0-1		0		1		0.5-1		1						?		1		1	
	No. of ECG.*		15		1				3		1						1		1		1	
	Seham[6]	I	0-1.5		0-1.5		0-1		1-2		1		0.4-0.5		1-1.5		1-1.5		1-1.5		0.5-2	
		II	0-2		0-2		0-2		1-2		1-1.5		0.5-2		0.5-3		2-3		0.5-2.5		1.5-2	
		III	0-2		0-0.9		0-1.5		0-1		0.5-1		0.5		0.5-2		1		0.5-1.5		0.5-2	
	No. of ECG.*		26		8		5		2		2		2		3		3		5		4	
	Lincoln and Nicolson[8]	I											0.5-2	1.5	0.5-3	1.4	0-3	1.3	0.5-3	1.2	0.5-3	1.2
		II											1-4.5	2.1	1-3	1.7	0-3.5	1.8	0.5-3.5	1.6	0.5-3	1.6
		III											0-3.5	1.2	0-3	0.9	0-3	1.2	0-2.5	0.9	0-3	1.5
	No. of ECG.*												9		40		57		58		68	
	Present series	I	0.5-2	0.97	0.5-2	0.96	0.5-2	1.3	0.3-2	1.0	0.5-1.5	0.97	0.5-2	1.0	0.5-2	0.95	0.5-1.5	0.98	0.5-1.8	0.92	0.5-2	1
	Burnett and Taylor	II	0.5-2	1.2	0.5-3	1.4	0.5-2	1.3	0.5-3	1.4	0.5-2	1.3	0.85-2	1.2	0.5-3	1.3	0.5-2.5	1.2	0.3-2	1.2	0.2-3	1.1
		III	0.2-2	0.76	0-2	0.77	0.3-1.5	0.75	0.3-2	0.8	0.3-2	0.75	0.2-1	0.7	0.2-2	0.7	0.3-1	0.7	0.2-1	0.6	0.2-1	0.67
	No. of ECG.*		178		140		84		87		146		129		100		81		81		80	
Q	5	I mm.	0-6		0		1		0-3		0						2		0			
		II	0-6		3		6		0-6		2						1		0.5			
		III	1-10		6		1		2-4		3						3		3			
	6	I	0-2		0-1		0-1.5		0-1		0-1		0.5-1		0-1.5		0-1		0-1			
		II	0-3		0-2.5		0-4		1		0.5-2		0-0.5		0-0.5		0-1		0-2			
		III	0-4		0-1.5		0-5		2		1		0		0-1.5		?-0.5		0-3			

*The figures for the number of electrocardiograms at each age period remained the same for each wave and are not repeated.

†Figures for the ninth through the eleventh years are not included in this table as the small number of individual cases did not justify an average.

‡For differences between boys' and girls' ranges see charts in Figs. 1, 2, 3, 5, and 6.

TABLE I—CONT'D

WAVES	AUTHORS	AGE	3 WK. TO 6 MO.		7-12 MO.		13-18 MO.		19-24 MO.		2-3 YR.		3-4 YR.		4-5 YR.		5-6 YR.		6-7 YR.		7-8† YR.	
		LEADS	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.
	8	I											0-3	1.3	0-3.5	0.8	0-4	0.85	0-3	0.8	0-3.5	0.65
		II											0-3	1.3	0-4	0.8	0-4	0.9	0-4	0.7	0-3	0.6
		III											0-6	2.2	0-7	1.3	0-5.5	1.4	0-5	1.3	0-4	0.85
	Present series	I	0-3	0.3	0-3	0.29	0-2.5	0.28	0-6	0.57	0-4	0.4	0-4	0.5	0-4	0.4	0-4	0.34	0-1.5	0.16	0-1.8	0.26
		II	0-7	1.4	0-6	1.4	0-6	1.4	0-5	1.2	0-3	1	0-3	0.95	0-5	1.1	0-4	0.92	0-4	0.6	0-2	0.6
		III	0-10	2.9	0-9	3.8	0-8	3.4	0-7	2.4	0-7	2.3	0-4.5	1.9	0-5	1.3	0-4	1.6	0-4	1.4	0-3	1
R	5	I mm.	3-18		7		6		1-9		6						9		12		16	
		II	7-18		18		8		10-13		7						12		14		13	
		III	5-14		12		9		6-8		6						5		4		3	
	6	I	1-6		2-6		3.5-11		0.4-10		4		3		4-6		5-7		5-9		2-8	
		II	0-10		1-10		4-17		7		7-7.5		5-12		6-12		6-8		7-22		7-11	
		III	1-15		0-7		4-10		4-6		5-5.5		2-6		4-6		2-5		0-21		4-8	
	8	I											5.5-15	9.9	6-20	10.4	4-16.5	9.9	5-16	9.5	5-18	9.7
		II											8-32	15.9	8-23	14.3	4-26.5	15	6-25	13.7	7-24	12.3
		III											5-31	10.9	2-23	10.5	2-24	11.2	3-24	10.6	3-26	10.5
	Present series	I	1-14	6.2	1-15	7.7	3-17	7.6	2-17	7.9	2-16	6.9	2-17	6.4	2-15	6	2-12	5.6	2-14	6	2-13	5.5
		II	1-20	10.2	2-23	11.6	2.5-24	11.1	1-19	11.4	2-19	11.2	3-23	11.8	3.5-19	12.1	3.5-25	12.2	5-30	12	4-24	12.5
		III	1-20	9.5	1-22	9.2	2-17	8.3	1-18	8	1-17	8.4	2-17	8.5	1-19	9.7	2-20	9.8	1-27	8.9	1-19	9.4
S	5	I mm	2-11		5		2		3-7		4						2		2.5		0	
		II	1-5		4		0		0-5		2						1		1		0	
		III	0-16		3		0		0-3		0						0		3		0	

TABLE I—CONT'D

WAVES	AUTHORS	AGE	3 WK. TO 6 MO.		7-12 MO.		13-18 MO.		19-24 MO.		2-3 YR.		3-4 YR.		4-5 YR.		5-6 YR.		6-7 YR.		7-8† YR.	
		LEADS	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.	RANGE	AV.
	6	I	1-8		0-3.5		0-2		2		0-1.5		0.5-1		0-4		0-3		0-3		0-4	
		II	0-8		0-3		0-3.5		2		0-2		0.2-3		1.5-4		1-4		0-2		1.8-4	
		III	0-8		0-2.5		0-1.5		1-2		0-0.5		0.5-1		0-2		2-4		0-2		0-1.5	
	8	I																				
		II											0-6.5	2.9	0-6	2.2	0-4.5	1.7	0-7	2.1	0-5	1.7
		III											1-7	3	0-5	2.3	0-7	1.9	0-7	2	0-5	2
													0-7	1.7	0-4	1.8	0-5	1.2	0-9	1.3	0-7.5	1.4
	Present series	I	0-15‡	4.2	0-11	4	0-13	6	0-8	3.2	0-13	2.9	0-6	2.3	0-7	2 3	0-7	2.5	0-9	2.2	0-8.5	1.8
		II	0-6	2	0-9	2.1	0-6	1.7	0-7	1.8	0-6.5	1.9	0-5	1.6	0-5	1.4	0-5	1.3	0-9	1.7	0-6	1.6
		III	0-5	1.2	0-8	3.8	0-9	6	0-9	1	0-7.5	0.76	0-8	0.93	0-8	0.7	0-8	0.75	0-6	0.8	0-7	0.9
T	5	I mm	1-6		3		4		2-7		3						1.5		3		4	
		II	1-5		2		2		1-4		3						2		2		4	
		III	0-5		1		2		1-2		1						?		1		1	
	6	I	0-3		0-2		1-6		2-3		1		2		3-5		2-4		4-5		2-7	
		II	0-6		1-3		1-5		1.5-3		2		4-5		3-4		2-6		3-6		3-9	
		III	0-5		0-1		0-2		0-2		0-1		1		1-1.5		3		1-4		2-4	
	8	I																				
		II											2-5	3.6	1-6	3.4	0-6.5	3.4	1-6	3.2	1-6	3.2
		III											1-7	3.4	1-5.5	3.4	0.5-7	3.6	0-5.5	3.5	1-6	3.4
													1-4	2.1	0-2.5	1.1	0-4	1.7	0-5.5	1.5	0-4.5	1.4
	Present series	I	0.5-7	2.3	0.5-6	2.8	1-6	2.7	1-6	3	1-6	2.7	1.5-5	2.9	1-5	2.7	1-5.5	3	1-6	2.8	1-6	3
		II	0.7-6	2.7	1-7	3.2	1-6	3.2	1-6.5	3.2	1-7	2.8	1.5-6	3.2	1-7	3.2	1-7	3.6	1-6	3.3	2-8	3.9
		III	0-4	0.91	0-3	1.1	0-4	1.2	0.3-3	1.1	0.5-3	1.2	0.2-3	0.91	0.2-2	0.96	0.2-3	1	0.2-3	0.98	0.2-1	1.3

than in the boys. As shown in Fig. 1, in girls the upper limit of 3 mm. was observed in four age groups while 2.5 mm. was noticed only once in boys. Further it shows the variation in range was less evident in Lead III than in the other two leads. After the tenth year there appeared to be less variation in all leads, especially in Lead I. For amplitude measurements as observed by other workers see Table I.

Notching, which first appeared in the third and fourth years, was noted in 195 or 15.2 per cent of our records. P_1 was notched in 42, or 3.2 per cent; P_2 in 49, or 3.8 per cent; and P_3 in 104, or 8.15 per cent; of the electrocardiograms. A number of previous workers[3, 6, 8, 9] report a split or notched P-wave as occurring in childhood. There are likewise several references to this occurrence in the adult electrocardiograms. This has been mentioned frequently as associated

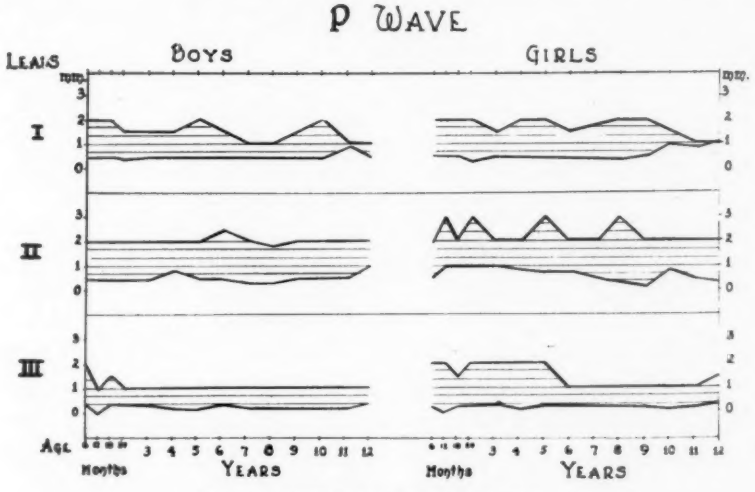

Fig. 1.—Amplitude range in P-wave.

with rheumatic heart disease, especially in the presence of mitral stenosis. Pardee[11] appears to be uncertain as to its meaning in the adult electrocardiogram. We would point out that the occurrence of notching of the P-wave in 15.2 per cent of average healthy children casts added doubt upon this finding as indicative of a lesion of the mitral or any other valve.

Diphasic forms which paralleled the notching were observed in P_2 in 6, or .047 per cent, and in P_3 in 46, or 3.6 per cent, of our records. Inversion of P_3 which appeared in the earliest records and throughout the series was noted in 133, or 10.4 per cent, of our records. After form changes in the P-wave had once appeared, we were unable to observe any age in which they were especially evident.

Summary.—The P-waves showed higher and lower amplitudes than in the adult and were more frequently high in girls than in boys.

However, the average of all waves in the three leads throughout the age period did not show any notable departure from the averages observed in the adult electrocardiogram.

Diphasic forms occurred in Leads II and III and notched forms in all leads. Inversion which occurred only in Lead III was found in the earliest records and totaled 133, or 10.4 per cent, in the entire series.

THE Q-WAVE

The Q-wave, representing the beginning of the ventricular complex, is not always present but is quite often seen in the electrocardiogram of early childhood. In our series the Q-wave when present was deeper in all leads in boys than in girls and diminished with age. Q_3 was

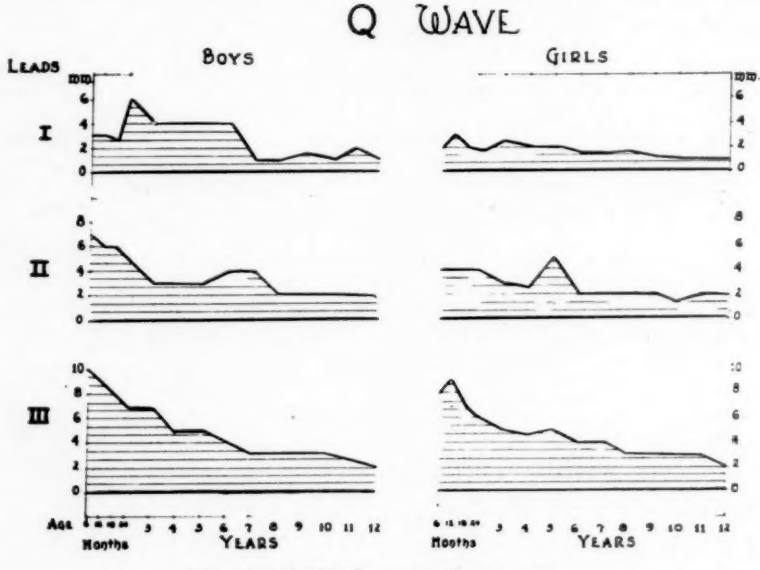

Fig. 2.—Amplitude range in Q-wave.

greater than Q_1 and Q_2. Both facts agree with the data of Lincoln and Nicolson.[8] In Leads I and III a marked decrease came at seven years in the boys while the decrease in the girls was more gradual. Q_3 showed slurring and notching in three electrocardiograms.

Reference to Fig. 2 will show the observed amplitudes of Q-waves in the three leads. In our series of normal electrocardiograms the Q-wave frequently exceeded in amplitude 25 per cent of the largest upward deflection of the QRS complex shown in any lead—the criterion employed in determining abnormally large Q-waves in the adult electrocardiogram.[11]

Summary.—The Q-waves diminished with age and were slightly deeper in boys than in girls. Q_3 showed the most gradual decrease in amplitude. Large Q-waves occurred in average healthy children.

THE R-WAVE

The R-wave is the main upward deflection of the ventricular complex. Linetsky[12] found that in adults the R-wave became higher with age and with increase of heart size. Previous workers, already cited, have shown the tendency for R-waves to be higher in the child than in the adult. For detailed amplitude measurements of these authors see Table I.

Amplitude.—Our records (Fig. 3) show that the R-wave observed in any given electrocardiogram may occasionally be lower or higher

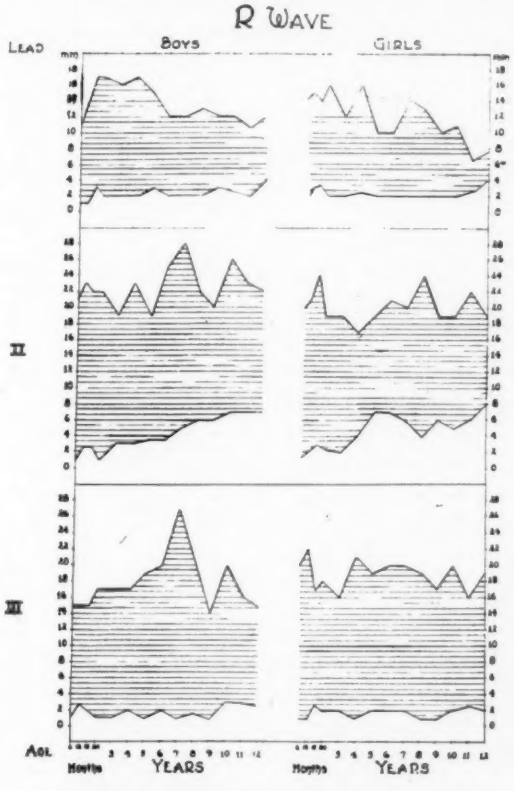

Fig. 3.—Amplitude range in R-wave.

than the usual adult standards. (Heart Committee,[10] 5 mm. to 20 mm.; Pardee,[11] 7 mm. to 17 mm.; Burnett and Piltz,[13] 8 mm.) Out of our entire series 137 records representing 55 individual cases were 17 mm. or over, while 98 records representing 44 cases were 7 mm. or below, the lowest being 3 mm. in two cases. Our curves show that when high or low R-waves were present in one record there was a tendency for the successive records to show the same thing. In boys the range of variation seemed to be somewhat greater than in girls but without any significant age difference. The average figures show that R_2 was

higher than R_1 or R_3. Waxing and waning, i.e., at least a 2 mm. variation in the height of the R-wave, was found in 69, or 5.4 per cent, of our series.

Slurring and Notching.—The term "slurring" is used whenever a thickening of either limb of the R-wave occurs clearly separated from the base line. R_1 was slurred 145 times, or in 11.1 per cent of our series. In 21 of these records R_2 or R_3 was also slurred. Of 87, or 6.8 per cent, showing slurring in R_2, 20 showed slurring in an additional lead while 67 showed slurring in only this lead. R_3 showed the largest number of variations. It was slurred in 225 records, or 17.6 per cent; out of which 31 records showed slurring in two other leads.

The term "notching" is used when there is a definite spike in any portion of the wave not adjacent to the base line. This was found in 7 records in Lead I, in 4 records in Lead II, and in 45 records in Lead III. In some records R_3 was notched in one complex with an *M* or *W* form in another.

M and W Forms of QRS Waves and Their Modifications.—Throughout this study we have used this term to apply to R- or S-waves which were so notched as to present roughly an *M* or *W* appearance. We did not lay down any exact criterion as to the height or depth of this complex or whether all were above or all were below the base line. Since the completion of the study of these curves, we have noted a report by Edeiken and Wolferth[14] on this form of QRS complex in which the authors have employed rather rigid criteria. We then made a somewhat limited search of various works on this subject and were surprised to find that a term so generally used appears to our knowledge in only one text, namely, in Neuhof's,[15] and that his criteria agree with ours. Neuhof presented some experimental evidence that purely physical factors may account for this type of split waves and that alone they should not be used as evidence of myocardial disease in the adult. In our series *M*- or *W*-form R_3-waves were noted in 35, or 2.7 per cent, of our records. The succeeding records may have been notched, *M* or *W* form, or possibly changed to an inversion of the R-wave.

Inversion of R-Wave.—The objection to this term is recognized, but at least in records of the age periods under discussion we are unable to advance a better term. In many of these records the chief downward deflection seems to be neither Q nor S. Inversion of the R-wave occurred only in Lead III and was present in 23, or 2 per cent, of our electrocardiograms. One hundred and twenty-four, or 9.7 per cent, of our records which showed notching, *M* or *W* forms, or inversion of R_3 were taken on thirty-five boys and nineteen girls. This indicates that the presence of one of these forms may be followed by one

or more of the associated forms in subsequent records. In nine cases the R_3 was found under two of the above classifications while in four cases under all three.

In Fig. 4 we present various modifications of the *M* and *W* forms. In *a* we show the customary form; in *b* the *M* and *W* appearance is less evident, but on comparison with curves in *a* there is a marked similarity. In *c* the QRS complex does not impress one as belonging to either form, and yet comparison with *b* shows a likeness. In all of these we are unable to classify accurately the various components of the

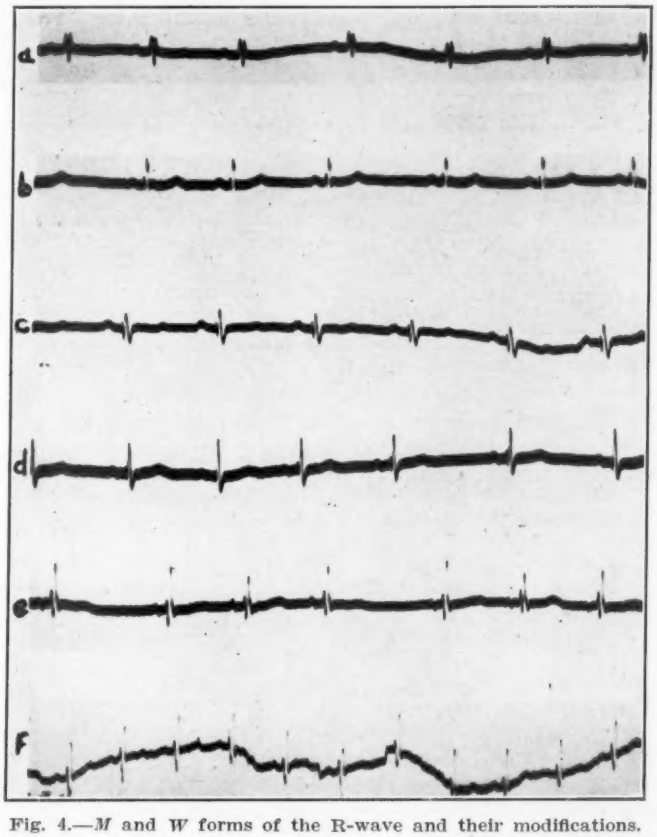

Fig. 4.—*M* and *W* forms of the R-wave and their modifications.

complex. How should one classify the first upward wave if the succeeding downward deflection is a Q-wave, or are we dealing with an inversion of all waves? If this explanation is adequate, there would be one remaining deflection unaccounted for. In addition to these changes, we show some variations in which *M* or *W* forms are not evident, but in which there is continuously or intermittently an extra and unclassified deflection. In *d* there is inconstantly an upward deflection preceding the R-wave. In *e* and *f* this is more marked, and in *f* succeeded by a deep Q-wave which shows rhythmical increase in depth.

Pardee[11] in his latest edition describes these variations in the QRS complexes. He prefers the term "vibratory" since many of these do not approximate closely an *M* or *W* and considers these not uncommon in Lead III.[16]

Wiggers[17] occasionally noted this "initial splintering" in normal adults and attributed this to "slightly unequal excitation of the two ventricles, the bio-electrocardiograms of which do not fuse into one smooth groove." The relative size changes are due to changes in the electrical axis with respiration. He labels these split or diphasic initial complexes and does not attach any significance to them.

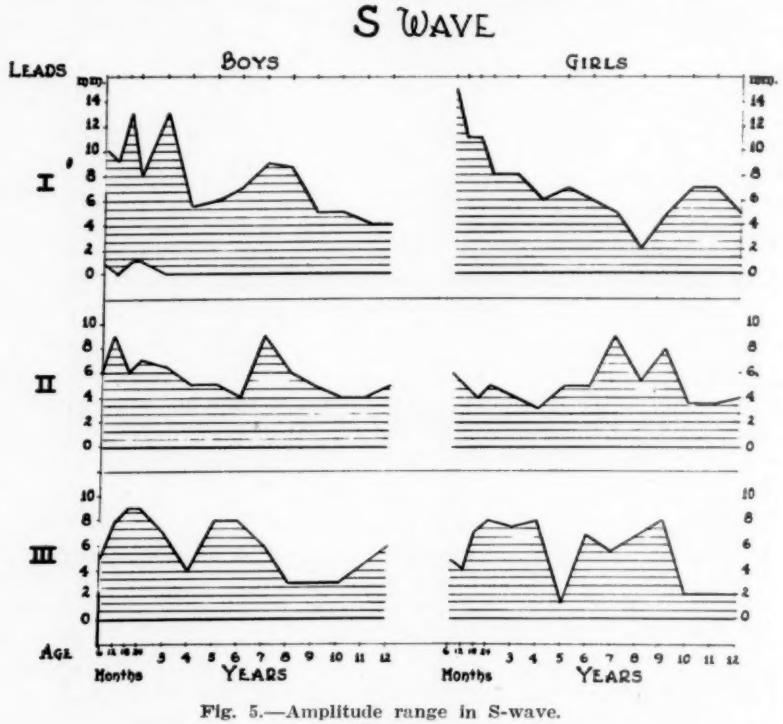

Fig. 5.—Amplitude range in S-wave.

Wilson[18] finds that they are difficult to classify or label but feels that the QRS group must be treated as a unit and that the letters *Q, R,* and *S* are to be used separately only for the purpose of description.

McGinn and White[19] discussed this inconsistency of nomenclature in a "Note on Nomenclature" in a study of the duration of the QRS complex. They suggest that the QRS wave may be described as consisting of plus and minus deflections extending so many millimeters above or below the base line without any arbitrary and often misleading attempts to label the individual deflections by exact letter. This method has the merit both of simplicity and accuracy.

Summary.—All R-waves may be higher or lower than in the usual adult standards. R-waves showed slurring in 457, or 35.8 per cent,

and notching in 56, or 4.3 per cent. *M* and *W* forms (2.7 per cent) and inversions (2 per cent) of R_3 were observed. It was difficult to classify portions of the QRS complex.

THE S-WAVE

Our series (Fig. 5) shows a decrease in size with age in boys and girls in all leads, but most marked in Lead I. Minor variations in amplitude occur independent of age or sex. The suggestion of Lincoln and Nicolson[8] regarding an increase in left ventricular activity shown by S_3 increase is not confirmed by our series. S_1 was slurred eleven times in our series and S_3 in six records, while Lincoln and Nicolson noted S_3 notched in twenty-two cases and split in six cases. (See Table I for amplitude measurements of other authors.)

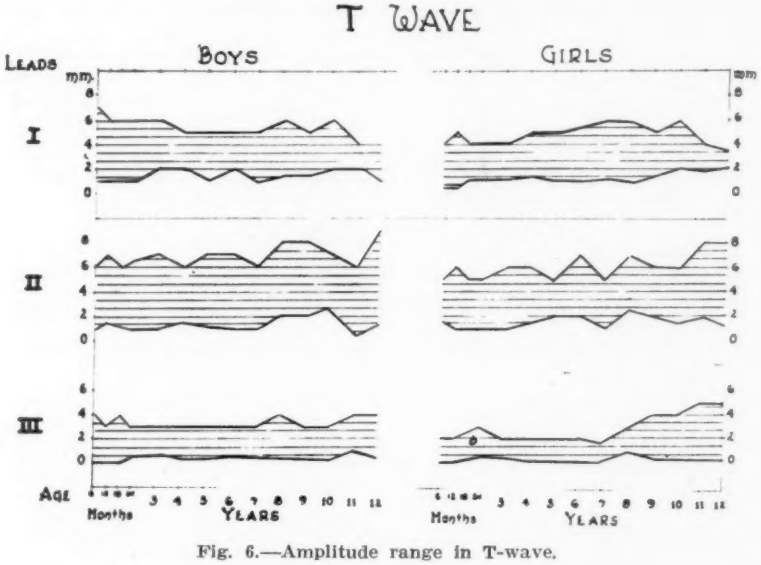

Fig. 6.—Amplitude range in T-wave.

THE T-WAVE

Our observations beginning with three-week-old infants show a well-defined T-wave in Leads I and II and usually in Lead III although of low voltage. (See Table I for comparison of figures of other authors.)

In our series Lead I was similar in both boys and girls but was usually higher than the adult standard of 5 mm. This was more marked in Lead II where it reached an amplitude of 8 mm. both in boys and in girls. T_3 was in general somewhat lower in both. These facts may be observed in Fig. 6.

In early, middle, and late childhood and adult life the T-wave, especially in Lead III, may show susceptibility to external influence. In our series there are several records in which T_3 became inverted

when the child changed from the recumbent to the sitting position. This change in posture probably has an effect upon the heart similar to that which occurs when there is a "shift to the right" since the mediastinal structures are extremely flexible at this age. Winternitz[20] believes that T_3 inversion in the adult indicates pronounced right heart hypertrophy, but most observers attach only slight if any importance to inversion occurring solely in Lead III in the adult electrocardiogram; certainly the T-wave in the adult is much less stable than the other deflections. A study of the electrocardiographic changes with shift in position is being made and will be subsequently reported.

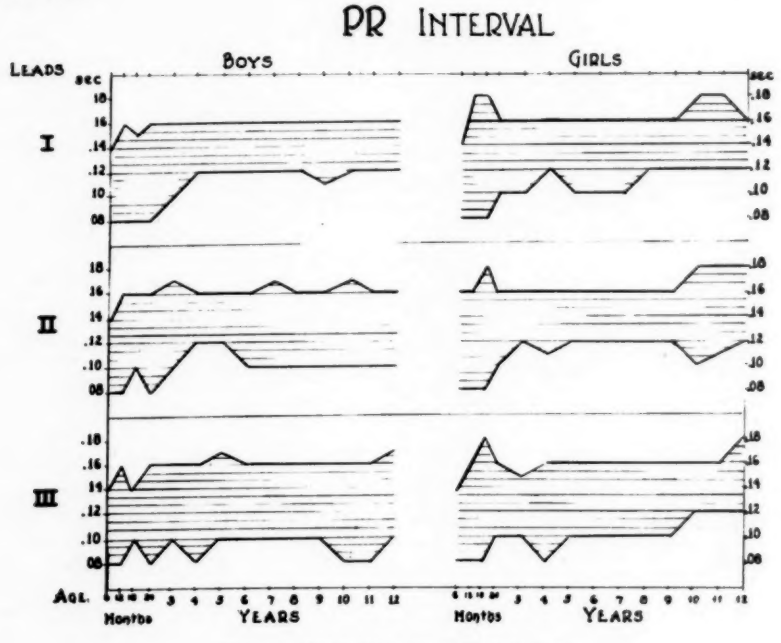

Fig. 7.—Variations in P-R intervals.

Forms.—Lincoln and Nicolson[8] have described the following forms of the T-wave: (1) a fairly steep rise from the R-S complex with a blunt peak and an abrupt drop; (2) the wave arising immediately from the R or S terminal at the base line with no S-T interval; and (3) the origin of the T deflection starting directly from the descending limb. All of these forms appeared in our series.

An inverted or a diphasic T-wave occurred only in Lead III. Inversion was seen in 242, or 18.9 per cent, of our records. Of these 140 were from boys and 102 from girls. The maximum frequency was found in the fourth and fifth years, with a decrease until the eleventh year. A diphasic T_3 was seen in only ten records.

Summary.—Well-defined and high T-waves were observed in Leads I and II. T_3 was usually of low voltage. Inversion was found only in T_3. It appeared in 242, or 18.9 per cent, of the records.

THE P-R INTERVAL

A more rapid conduction time for children than for adults and an average of 0.136 second have been noted by previous authors.[3, 6, 8] An average of our series for the first eight years gave the slightly lower figure of 0.126 second. The extremes in the duration of the P-R interval at different age periods in boys and girls may be seen in Fig. 7 as 0.16 and 0.17 second, except in two instances in the second and third age group when one girl showed a duration of 0.18 second. In the later age groups all leads in girls approximated 0.18 second.

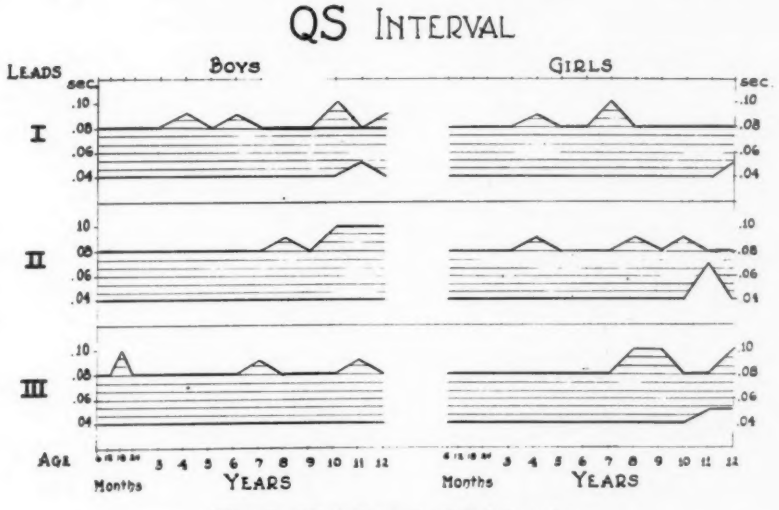

Fig. 8.—Variations in Q-S intervals.

This interval varies in different leads from this high point to as low as 0.08 second. These shorter intervals seem to bear no relation to sex or age. No explanation for this is advanced.

Summary.—The auriculoventricular conduction time varied from 0.08 to 0.18 second and averaged 0.126 second for the first eight years.

THE Q-S INTERVAL

Previous reports[8, 6, 19] showed this conduction time from 0.06 second, upper limit 0.09, with no significant age difference. In our series (Fig. 8) a range of 0.04 to 0.08 second was usually found in this interval while adult standards are 0.081 to 0.10 second. However, 0.10 second was the upper limit in several age groups and appeared to bear no relationship to age or sex. The average in our series for the first eight years was 0.0549 second.

Summary.—The Q-S transmission time was shorter in the hearts of children.

THE S-T INTERVAL

A very definite age factor was found in the length of the S-T interval. This is seen on comparing Fig. 9 with Figs. 7 and 8. In the early age groups the range was from approximately 0.16 second to 0.28 second, whereas at the twelfth year it was from 0.24 second to 0.34 second. The lengthening of this interval was due obviously to a lengthening of systole at the later age periods. From a study of the Figs. 7, 8, and 9, it is evident that conduction time from the sinus

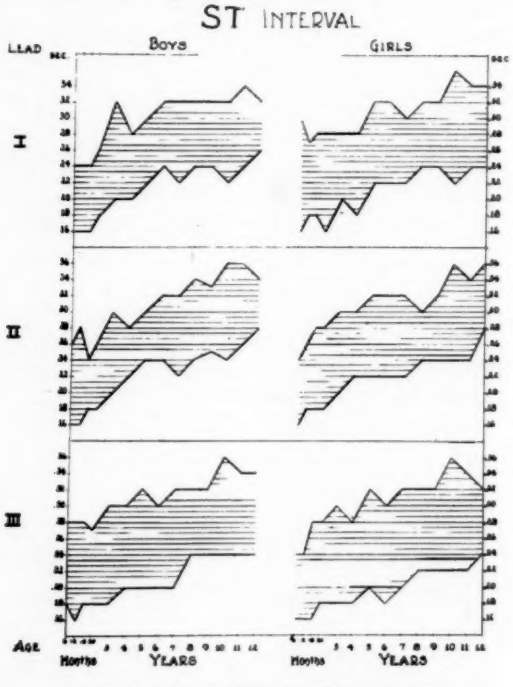

Fig. 9.—Variations in S-T intervals.

node to the Purkinje fibers appeared shortened throughout early and late childhood, but the duration of systole was markedly lengthened as age progressed.

Seham[6] gave an average of 0.213 second for the duration of this interval from one to five years of age while our average was 0.24 second from three weeks to eight years.

Summary.—A definite lengthening with age was observed in the S-T interval.

In Table II the minimum, maximum, and average intervals observed in our series are presented.

HEART RATE

It is an accepted fact that a child's heart beats more slowly as he grows older. Lincoln and Nicolson[8] in their series showed that the girls had a more rapid heart rate than boys up to the age of seven years. Our series showed that the girls' heart rates were more rapid from the first month to the fifth year when the boys' rates were more rapid.

TABLE II

MINIMUM, MAXIMUM, AND AVERAGE OF THE P-R, Q-S, AND S-T INTERVALS

AGE	LEADS	P-R		Q-S		S-T	
		RANGE MIN. MAX.	AV.	RANGE MIN. MAX.	AV.	RANGE MIN. MAX.	AV.
3 wk. to 6 mo.	I	0.08 - 0.14	0.107	0.04 - 0.08	0.048	0.16 - 0.30	0.203
	II	0.08 - 0.16	0.11	0.04 - 0.08	0.048	0.16 - 0.26	0.207
	III	0.08 - 0.14	0.109	0.04 - 0.08	0.05	0.16 - 0.24	0.199
7 mo. to 12 mo.	I	0.08 - 0.16	0.114	0.04 - 0.08	0.052	0.16 - 0.27	0.207
	II	0.08 - 0.16	0.12	0.04 - 0.08	0.052	0.16 - 0.28	0.214
	III	0.08 - 0.16	0.114	0.04 - 0.08	0.055	0.16 - 0.28	0.208
13 mo. to 18 mo.	I	0.08 - 0.18	0.118	0.04 - 0.08	0.056	0.16 - 0.28	0.219
	II	0.08 - 0.18	0.119	0.04 - 0.08	0.056	0.18 - 0.28	0.219
	III	0.08 - 0.18	0.116	0.04 - 0.10	0.05	0.16 - 0.28	0.216
19 mo. to 24 mo.	I	0.08 - 0.16	0.119	0.04 - 0.08	0.054	0.16 - 0.28	0.226
	II	0.08 - 0.16	0.123	0.04 - 0.08	0.053	0.18 - 0.28	0.23
	III	0.08 - 0.16	0.117	0.04 - 0.08	0.052	0.18 - 0.28	0.224
Third year	I	0.10 - 0.16	0.128	0.04 - 0.08	0.052	0.20 - 0.28	0.238
	II	0.10 - 0.17	0.13	0.04 - 0.08	0.052	0.20 - 0.30	0.243
	III	0.10 - 0.16	0.12	0.04 - 0.08	0.052	0.18 - 0.30	0.246
Fourth year	I	0.12 - 0.16	0.13	0.04 - 0.09	0.053	0.18 - 0.28	0.256
	II	0.11 - 0.16	0.13	0.04 - 0.09	0.05	0.22 - 0.30	0.25
	III	0.08 - 0.16	0.126	0.04 - 0.08	0.054	0.18 - 0.30	0.248
Fifth year	I	0.10 - 0.16	0.135	0.04 - 0.08	0.054	0.22 - 0.32	0.257
	II	0.12 - 0.16	0.135	0.04 - 0.08	0.054	0.22 - 0.32	0.26
	III	0.10 - 0.17	0.131	0.04 - 0.08	0.056	0.20 - 0.32	0.251
Sixth year	I	0.10 - 0.16	0.14	0.04 - 0.09	0.057	0.22 - 0.32	0.264
	II	0.10 - 0.16	0.139	0.04 - 0.08	0.058	0.22 - 0.32	0.267
	III	0.10 - 0.16	0.132	0.04 - 0.08	0.06	0.20 - 0.30	0.255
Seventh year	I	0.10 - 0.16	0.143	0.04 - 0.10	0.057	0.22 - 0.32	0.264
	II	0.10 - 0.17	0.138	0.04 - 0.08	0.06	0.22 - 0.32	0.268
	III	0.10 - 0.16	0.132	0.04 - 0.09	0.062	0.20 - 0.32	0.261
Eighth year	I	0.12 - 0.16	0.142	0.04 - 0.08	0.058	0.24 - 0.32	0.273
	II	0.10 - 0.16	0.142	0.04 - 0.09	0.064	0.24 - 0.34	0.274
	III	0.10 - 0.16	0.139	0.04 - 0.10	0.064	0.22 - 0.32	0.271

In checking with the physical examination, the heart rate was usually slower when calculated from the electrocardiogram than from physical examinations. The above mentioned authors found the opposite to be true, attributing the cause to some fear of the procedure of making a cardiogram. From seven months until two years of age, when the children are most difficult to handle, the heart rate was a little more rapid than during physical examination, but after they had overcome their fears the heart rate remained slower. At the fifth year the low rate was 68 in girls, and this decreased to 58 the last

four years (nine to twelve years, inclusive). The record which showed the heart rate of 58 was that of a girl whose first record at seven years four months showed a rate of 64. The most rapid heart rate of 195 was in a girl three months old. The rate of her succeeding records decreased to 88 at three years three months.

As a means of determining to what the decrease in the heart rate is due, whether prolonged contraction solely or prolonged contraction and diastole, we noted the most rapid, moderate, and slowest heart rates in boys and girls in eight age groups. We found that the increase in diastole or T-P interval was responsible for the slower rate. The time of diastole did not change more than 0.04 second up to six years while a variation of 0.10 second was observed in the eleventh year.

Summary.—The decrease of the heart rate with age paralleled the increase in diastole as shown by the T-P interval.

Table III presents the slowest, most rapid, and average heart rates observed in our age groups.

TABLE III

THE SLOWEST, MOST RAPID, AND AVERAGE HEART RATES

HEART RATE	3 WK. TO 6 MO.	7 MO. TO 12 MO.	13 MO. TO 18 MO.	19 MO. TO 24 MO.	3RD YEAR	4TH YEAR	5TH YEAR	6TH YEAR	7TH YEAR	8TH YEAR
Slowest	115	92	90	82	65	80	68	69	62	64
Most rapid	195	190	178	171	166	145	138	111	105	118
Average	142.7	141.3	123.7	116.1	107.9	101.1	95.7	89.7	88.6	83.7

SINUS ARRHYTHMIAS

Previous reports[6, 8] show that sinus arrhythmias are found more frequently in older children. Krumbhaar[5] considered a record to show sinus arrhythmia when the difference between the shortest and longest heart cycle was 0.10 second or more.

Accepting Krumbhaar's criterion, as the other workers have, we found 279 records, or 21.8 per cent, showing as much variation as this. The earliest evidence of sinus arrhythmia was seen in a boy and in a girl fourteen months of age. From that age on there was a constant increase in the frequency of incidence until the maximum percentage was reached in the tenth and eleventh years. This suggests that this is the period of childhood in which vagus activity becomes fully developed, since it is generally accepted that this type of activity is due to a varying degree of vagus control.

Summary.—Two hundred and seventy-nine, or 21.8 per cent, of our records showed sinus arrhythmia, the greatest incidence being in the tenth and eleventh years.

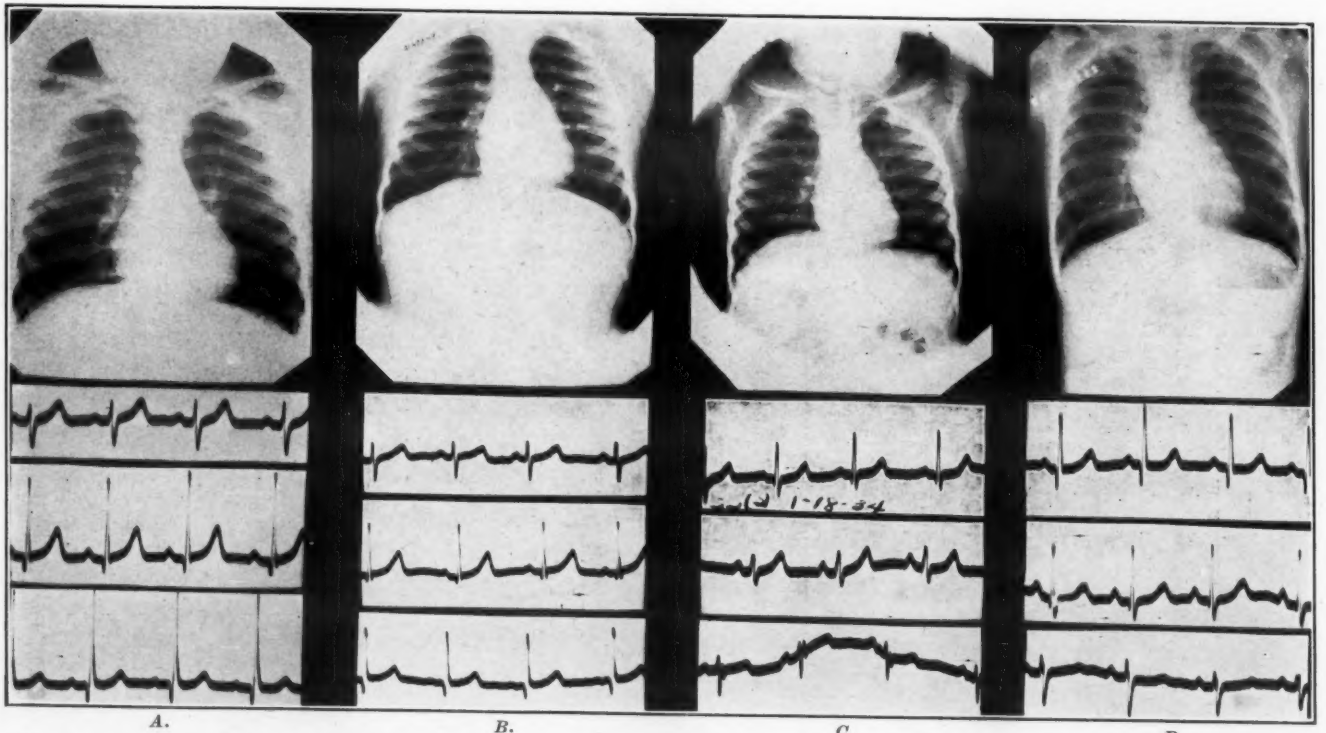

Fig. 10.—Electrocardiograms and heart roentgenograms on four children. The electrocardiograms show:
A, a right axis deviation on a boy aged seven years six months.
B, a suggestion of right axis deviation on a four-year-old girl.
C, left axis deviation on a girl three years three months of age.
D, a suggestion of left axis deviation on a boy aged five years seven months.
Note that none of the chest roentgenograms indicates preponderance of either ventricle.

AXIS DEVIATION

The term "right axis deviation" as defined by the Heart Committee[10] includes those electrocardiograms in which the main deflection of the QRS group in Lead I is downward and R_3 is larger than R_2 (Fig. 10 *A*). A number of earlier workers[1, 2, 5, 6] have noted a deep S, or stressed the frequency of "right preponderance" in the first few months. In our series of records 58, or 4.5 per cent, were included under this term. Those records with a deep S_1, but R_2 and R_3 balancing, are considered as suggestive of right axis deviation (Fig. 10 *B*). Sixty, or 4.7 per cent, of our cases may be so included.

Table IV shows the age occurrence of right axis deviation in the first six months.

TABLE IV

AGE	BOYS			GIRLS		
	NO. OF CASES	RT. AXIS DEV.	SUGG. RT. AXIS DEV.	NO. OF CASES	RT. AXIS DEV.	SUGG. RT. AXIS DEV.
1 to 3 mo.	58	12	9	63	16	6
4 to 6 mo.	29	2	1	28	2	3

The term "left axis deviation" may be applied to those records in which the main deflection in Lead III is downward and R_1 is larger than R_2[10] (Fig. 10 *C*). The suggestion of this deviation includes those in which R_2 was equal to or higher than R_1 but with the main deflection in Lead III downward (Fig. 10 *D*). Under left axis deviation thirty-five records, or 2.7 per cent, were included, while twenty-six, or 2.03 per cent, showed a suggestion of left axis deviation.

Summary.—Right axis deviation was most marked during the first three months, with a notable decrease during the period from four to six months. Left axis deviation occasionally occurred in average healthy children.

SUMMARY

1. The P-wave showed higher and lower amplitudes than in the adult. Diphasic forms occurred in Leads II and III and notched forms in all leads.

2. Q-waves were deeper in boys than in girls, and there was a more gradual decrease with age in girls than in boys.

3. R-waves may be higher or lower than usual adult standards indicate. R-waves showed slurring in 457, or 35.8 per cent of the records, and notching in 56, or 4.38 per cent. R_3 alone presented *M* and *W* forms and inversion. It is difficult to classify portions of the QRS complex.

4. S-waves decreased with age in all leads.

5. Well-defined and frequently high T-waves were observed in Leads I and II. T_3 was usually of low voltage. Inversion was seen only in T_3. It occurred in 242, or 18.9 per cent, of the cases in this lead.

6. Transmission time was shorter in hearts of children; as seen in the P-R and Q-S intervals. The S-T interval showed a definite lengthening with age.

7. Heart rates decreased with age.

8. Sinus arrhythmia was shown in 279, or 21.8 per cent, of our records and was seen most frequently in the tenth and eleventh years.

9. The greatest number of instances of right axis deviation was found in the first three months of life, with a notable decrease in the period of from four to six months. Left axis deviation occasionally occurred in average healthy children.

10. Our study indicates that normal standards must allow a wide range of individual variations in the electrocardiograms on healthy infants and children.

11. This study indicates the need for similar statistical studies through later childhood and adult life and suggests a greater variation in the normal adult electrocardiogram than is indicated by present accepted standards.

We desire to thank Dr. O. L. Huddleston and Dr. E. Durbin for assistance given in measuring some of these records and the staff of the Child Research Council for helpful suggestions.

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MINUTE VOLUME DETERMINATIONS IN MITRAL STENOSIS DURING AURICULAR FIBRILLATION AND AFTER RESTORATION OF NORMAL RHYTHM*†

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THE rôle played by the auricle in the work of the heart has been studied for many years. There have been different approaches to the solution to this problem, but all of them lead to approximately the same conclusions. The first method of approach was that of ventricular filling curves. In 1906 Yandell Henderson[1] stated that he could get very little if any change in the filling curves of the ventricle during auricular contraction. This work has since been severely criticized by Straub[2] and by Gesell,[3] who show definitely that the Marie tambour which Henderson used was not sensitive enough for the type of work he was doing.

In 1908 Hirshfelder[4] did some very interesting experiments on the subject. He first made ventricular filling curves in normal dogs which showed the following characteristics (Fig. 1 is a reconstruction of these curves): At the beginning of diastole, the ventricle filled very rapidly as shown by a very steep rise in the curve. Then, as the pressure between the auricles and the ventricles became equalized, this curve tapered off, so that for a short period of time, there was practically no filling. Simultaneously with auricular contraction, the filling curve again showed a steep rise and tapered off again just as before ventricular systole. The filling produced by the auricle in these normal dogs was approximately 20 per cent of the total diastolic filling of the ventricles. Hirshfelder then produced artificial mitral stenosis in these same dogs. He did this by passing a ligature around the mitral orifice in such a way that when the ligature was drawn tight, a stenosis was produced at this valve. The filling curve then took on a slightly different form. Because of the obstruction between the auricle and the ventricle, the ventricle did not fill as rapidly as in the normal dog, and therefore the curve was not as steep nor did it rise to as great a height as it did in the normal dog. Later in diastole when the pressures in the auricle and the ventricle became more nearly equal, a period was again reached when there was very little if any filling. When auricular contraction occurred, however, a considerable amount of blood was forced into the ventricles, as shown by a very rapid rise in the ven-

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tricular filling curve which led up to ventricular systole. In these dogs with mitral stenosis, the percentage of filling produced by the auricle was approximately 25 per cent as compared to the normal value of 20 per cent. He then carried on an experiment in the same way except that he faradized the auricles, causing them to fibrillate. When this occurred, the filling curve again started out just as it had in the preparation before fibrillation took place. However, as no auricular systole took place, there was no secondary rise in the curve and the ventricle never became as completely filled as it was previously. This showed then, rather conclusively, that the auricle contributed approximately 25 per cent to the filling of the ventricle in mitral stenosis and therefore, if the ventricular rates were equal, contributed approximately 25 per cent to the minute volume.

In 1910 Straub,[2] using the cat as the experimental animal, made a cardiometer in which the membrane on the tambour consisted of a soap

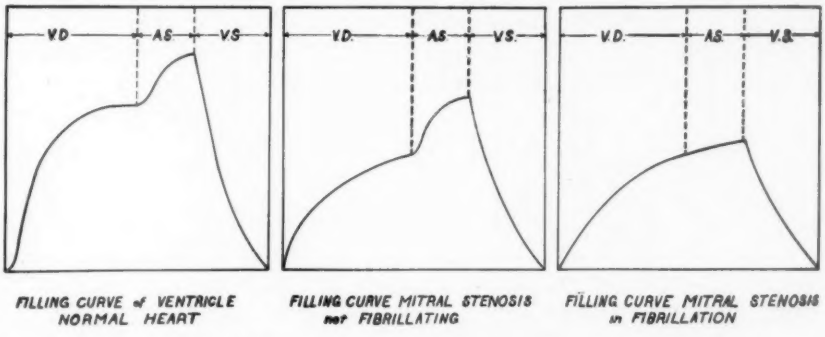

Fig. 1.—*V. D.*, ventricular diastole; *A. S.*, auricular systole; *V. S.*, ventricular systole. (Reconstructed from Hirshfelder's experimental curves.[4])

bubble. He photographed the movements of this soap bubble on a moving film. He found that the auricle contributed some 33 to 66 per cent of the filling of the ventricle.

In 1912 DeHeer[5] made similar ventricle filling curves and found that approximately 30 per cent of the filling of the ventricle was due to the auricle. In 1922 Wiggers and Katz,[6] with an improved method, found that the auricles contributed from 19 to 60 per cent of the filling of the ventricle and that the average contribution of the auricle was 35 per cent.

The second method of attack was made by means of blood pressure measurements. Gesell[3] in 1911 used a preparation in which he crushed the His bundle in a dog and used different rates of stimulation to the auricles and to the ventricles. He noticed definite changes in aortic pressures when different rates of stimulation of the auricle as compared with the ventricle were used. For instance, if he stimulated the auricle

thirteen times a minute and the ventricle twelve times a minute, he found that he could set up definite interference waves in the blood pressure, i.e., the maximum blood pressure occurred when the auricle contracted just before the ventricle and the minimum blood pressure curve when the auricle contracted during the ventricular systole. He also found that if the auricles were stimulated twice for each stimulation of the ventricle, the blood pressure was higher than that obtained when the auricles were stimulated at the same frequency as the ventricles. He came to the conclusion that the auricles were responsible for approximately 25 to 50 per cent of the minute volume of the heart.

The third method of approach was through minute volume determinations on animals before and during artificially produced auricular fibrillation. Lewis[7] in 1912 used dogs and cats and found that the auricular fibrillation caused a decrease in minute volume of approximately 20 per cent. He also found that the greater the rate of the ventricle following auricular fibrillation, the greater the loss in minute volume. This is borne out also by some work by Eyster and Swarthout,[8] using a similar method on dogs. They found that auricular fibrillation decreased the minute volume all the way from 15 to 79 per cent. In studying their tables, one finds that the 79 per cent decreases were in those dogs in which the ventricular rate became very rapid while the lower decrease in minute volume was in those dogs in which the rate was not so rapid. The last method of approach has been the determination of minute volumes in cases of auricular fibrillation in the human. Smith, Walker, and Alt[9] in 1930 found that, when normal rhythm was restored by the use of quinidine in patients with auricular fibrillation, the minute volume increased approximately 30 per cent.

In our work we have attempted to carry out this same method. We have limited ourselves to cases of mitral stenosis for two reasons. We chose cases of mitral stenosis because we believed that the dilatation and hypertrophy of the auricles in these cases would give us a greater difference in minute volume when the normal rhythm was restored and because it is of considerable importance to know whether the use of quinidine in mitral stenosis increases the mechanical efficiency of the heart by restoring normal auricular function. The method was carried out as follows: Patients with mitral stenosis with auricular fibrillation were either brought into the hospital or kept at rest at home. They were all given digitalis, and the ventricular rates were brought down to approximately 60 to 70 per minute. Those patients who were decompensated were allowed to compensate as far as possible under this regime. The compensation was checked by physical signs and by the use of vital capacity determinations. When no further improvement was possible under this regime, minute volume studies were begun. The minute volumes were determined by the Grollman[10] acetylene gas method,

a method which has yielded very excellent results in our hands. Minute volume determinations were made upon those patients whose ventricular rates had been brought down to 60 to 70 beats per minute and who were also compensated. Duplicate determinations were made on each case, and the average of these determinations was accepted as the minute volume of the patient while the auricles were fibrillating. These patients were then kept on the maintenance dose of digitalis. They were given quinidine. When the normal rhythm was restored, quinidine was reduced to a maintenance dose which, in our hands, amounts to 9 to 15 grains a day, and minute volume determinations were again made. The average of these determinations after quinidine medication was taken as the minute volume with the auricles beating regularly. In all, we have studied seventeen females and five males (Table I). The seventeen females had an average minute volume of 2.35 liters per minute during fibrillation. Of these, seven became regular, and the average minute volume of these seven after becoming regular was three liters per minute. This increase from 2.35 to 3 liters per minute is an increase of 27 per cent. The increase in the individual cases varied from 14 to 36 per cent, and the average increase in these seven cases was 26 per cent.

TABLE I

CASE	MINUTE VOLUME FIBRILLATING (LITERS PER MINUTE)	MINUTE VOLUME REGULAR (LITERS PER MINUTE)	PER CENT INCREASE
	Females		
M. A.	2.84		
H. B.	2.85		
I. C.	3.15	3.48	14
I. F.	1.28		
E. K.	2.60		
I. K.	2.26		
L.	2.03	2.77	36
C. L.	2.62	3.38	28
H. O.	2.67		
R.	1.95		
E. S.	2.00	2.62	31
A. S.	2.12	2.67	25
G. S.	2.38	2.90	21
M. T.	2.54	3.18	25
T.	1.74		
H. W.	2.38		
M. W.	2.55		
Average	2.35	3.00	27
	Males		
E. B.	2.64		
G. K.	3.75		
J. O.	3.85		
A. S.	2.25		
J. S.	2.41	2.87	19
Average	2.98		
Average increase for both males and females = 25 per cent			

Grollman[10] has stated that the average minute volume in females is 3.6 liters per minute. Returning now to our filling curves (Fig. 1), which we have reconstructed freely from Hirshfelder's experiments in mitral stenosis, we find that our results are in very good accord with his experiments on dogs. The normal heart with a minute volume of 3.6 liters per minute corresponds to the first curve. The hearts of Hirshfelder's experimental animals with mitral stenosis and with the auricles beating regularly have a somewhat decreased rise in the ventricular filling curve. We find the minute volumes of our patients with mitral stenosis in females averaging approximately three liters per minute or about 17 per cent less than the normal. Our cases of mitral stenosis with auricular fibrillation in females correspond to the third curve reconstructed from Hirshfelder's curves of experimentally produced mitral stenosis with auricular fibrillation. We find that the minute volume here corresponds to what one would expect from a study of those curves, namely, our figure to 2.35 liters per minute is approximately 22 per cent less than the minute volume in cases of mitral stenosis without auricular fibrillation.

The series of males has been much smaller. We have studied only five males with mitral stenosis and find that their average minute volume during fibrillation is three liters per minute, or about 25 per cent under the average for normal males as determined by Grollman. In only one of these males did the rhythm become regular, and his increase in minute volume was 19 per cent on becoming regular. Because of the small number of males, it is unjustifiable in this series to draw any conclusions from average values. However, it is very probable that if the series of males were as large as the series of females, the results would be the same.

Kohn and Levine[11] in a recent publication have stated the belief that the restoration of normal rhythm in auricular fibrillation does not increase cardiac efficiency. In view of our results, it is difficult for us to concur in this belief. We believe that these results prove definitely that at least in mitral stenosis the restoration of normal rhythm in auricular fibrillation is of definite value in increasing cardiac efficiency.

CONCLUSIONS

1. Results show that the minute volume in mitral stenosis is frequently definitely reduced.

2. The appearance of auricular fibrillation further reduces the minute volume in mitral stenosis by approximately 22 per cent.

3. The restoration of normal rhythm, by the use of quinidine, is of definite value in that it increases the minute volume by approximately 25 per cent. The increase in cardiac efficiency justifies the use of quinidine.

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TRANSIENT COMPLETE BUNDLE-BRANCH BLOCK

Report of Six Cases

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ELECTROCARDIOGRAMS exhibiting bundle-branch block are no longer of uncommon occurrence, but this condition is usually associated with advanced heart disease and, once established, is prone to persist for the remainder of the patient's life. Transient bundle-branch block occurs relatively infrequently, and a comparatively small number of such instances have been reported in the American literature. Wolff, Parkinson, and White[1] observed eleven cases of transient bundle-branch block in apparently healthy young people. Willius and Anderson[2] reported a case of transient, recurrent complete bundle-branch block, unique in certain respects, and were fortunate enough to have recorded the transition from the normal to the abnormal mechanism. They called attention to the infrequency with which bundle-branch block has been reported as a transient finding and in reviewing the literature mentioned three cases of transient incomplete bundle-branch block reported by Willius and Keith[3] in 1927, one case of transient complete bundle-branch block reported by Baker[4] in 1930, and two cases of a similar nature reported by Morris and McGuire[5] in 1932. This makes a total of seven cases in which there was a background of organic heart disease, and eleven cases in which no heart disease could be demonstrated.

In the course of the last year and a half transient bundle-branch block has been observed in five patients on the wards of the Wisconsin General Hospital and in one patient at the Madison General Hospital. Advanced heart disease was present in every instance, and in one case the finding followed a coronary thrombosis. These six cases form the basis of the present report.

Case 1.—H. M., a man aged seventy-three years, was admitted to the Wisconsin General Hospital, Jan. 13, 1933, for treatment of bilateral senile cataracts. There were no symptoms referable to the heart except for moderate shortness of breath on exertion.

Physical examination revealed a well-developed and nourished white elderly male. The radial arteries were moderately thickened, and the pulse was slightly irregular. The blood pressure was 130 systolic and 74 diastolic. The heart was moderately enlarged to the left. The sounds were of poor quality at all areas, and no murmurs were heard. A few moist râles were noted at both lung bases posteriorly.

The blood Wassermann reaction was negative. An electrocardiogram taken Jan. 18 (Fig. 1*A*) showed a left bundle-branch block, as well as other disturbances of the conduction mechanism. The P-R interval varied from 0.10 to 0.29 of a second, and the QRS interval averaged 0.15 of a second.

A diagnosis was made of immature bilateral senile cataracts, coronary heart disease with moderate cardiac enlargement, advanced myocardial degeneration, and left bundle-branch block. The patient was discharged Jan. 20, 1933, and instructed to return in three months for further observation and possible operation.

The patient was readmitted to the hospital April 25, 1933, having received no medical treatment in the interim. The physical examination was essentially the same as on the previous admission, but the electrocardiogram taken May 2, 1933 (Fig. 1*B*), showed a left axis deviation but no evidence of bundle-branch block. The P-R interval was 0.21 and the QRS 0.10 of a second. On May 3, 1933, a preliminary iridectomy was successfully performed on the right eye. Recovery was uneventful, and the patient was discharged May 10.

CASE 2.—Mrs. M. L., a woman of sixty-one years, was admitted to the Wisconsin General Hospital Nov. 27, 1933, with a chief complaint of shortness of breath which

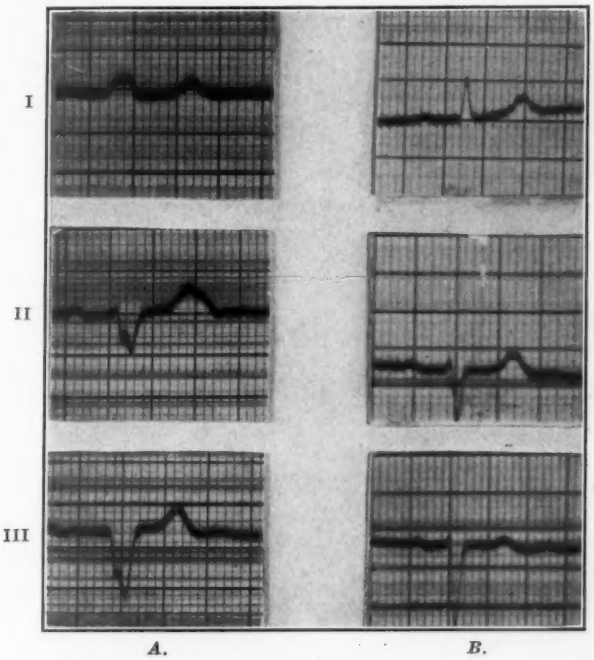

Fig. 1.—(Case 1.) Male, aged seventy-three years. *A*, electrocardiogram taken Jan. 18, 1933, showing left bundle-branch block. *B*, tracing taken May 2, 1933, showing left axis deviation but no bundle-branch block.

had been present for the preceding four years. She was known to have had an elevated blood pressure for several years. Five days before admission she became very ill with an attack of severe epigastric distress accompanied by marked shortness of breath and agonizing pain over the heart radiating to both sides of the neck. This attack lasted nearly twenty-four hours in spite of repeated hypodermic injections of morphine.

Physical examination revealed a well-developed and nourished woman of 61, obviously seriously ill. The skin was slightly cyanotic, and dyspnea was marked. The retinal arteries showed marked sclerosis, and the veins were definitely engorged. The radial arteries were moderately thickened; the pulse was reduced in volume and was regular at a rate of 50. The blood pressure was 155 systolic and 85 diastolic. The heart was moderately enlarged to the left, and the heart sounds were distant

and of poor quality. No friction rub could be detected. Fine moist râles were heard at both lung bases posteriorly, and there was moderate pitting edema of both lower extremities.

The blood Wassermann test was negative. The blood count showed 14,950 leucocytes. An electrocardiogram taken the day after admission (Fig. 2*A*) showed typical left bundle-branch block. There appeared to be a 2:1 A-V block in Lead I although the P-R interval was well within normal limits. In Leads II and III the P-wave occurred about midway between the QRS complexes. The QRS interval was 0.15 of a second. A diagnosis was made of coronary and hypertensive heart disease with recent coronary thrombosis, moderate cardiac enlargement, left bundle-branch block, and congestive failure, functional capacity Class III.

The patient was kept at complete bed rest and oxygen was administered per nasal catheter. One and one-half grains of aminophyllin were given three times daily by

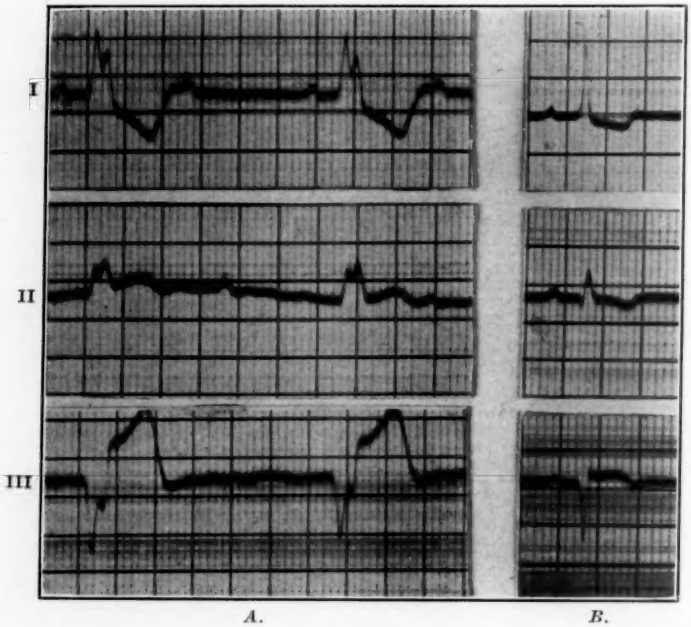

Fig. 2.—(Case 2.) Female, aged sixty-one years. *A*, electrocardiogram taken Nov. 28, 1933, showing typical left bundle-branch block. Coronary occlusion had occurred six days previously; 2:1 A-V block appears in the first lead. In Leads II and III a definite P-wave seems to appear only at a point about midway between the QRS complexes. *B*, tracing taken Dec. 4, 1933, two weeks after the coronary occlusion. Bundle-branch block has disappeared, but the deep Q_3, the S-T segment deviation, and the T-wave inversion are evidences of coronary involvement.

mouth. An electrocardiogram taken Dec. 4, 1933 (Fig. 2*B*) while the patient was receiving oxygen showed a return to normal rhythm and a complete absence of the bundle-branch block. However, a very deep Q_3, definite S-T segment deviation in Leads I and III, and inverted or diphasic T-waves in all leads, were characteristic of recent infarction. The oxygen was discontinued on December 6. By Jan. 15, 1934, all signs of congestion had disappeared. A third electrocardiogram taken Jan. 16, 1934, and the fourth one, taken a few days before dismissal from the hospital, showed the progressive changes commonly found following a coronary thrombosis, but bundle-branch block was not present after the first electrocardiogram. The patient was discharged from the hospital on Feb. 10, 1934.

CASE 3.—J. E. N., a farmer, aged sixty-six years, was admitted to the Wisconsin General Hospital July 12, 1933, for repair of an inguinal hernia. For some time he had been troubled with palpitation and shortness of breath on exertion and recently had frequently been awakened at night by severe attacks of shortness of breath, necessitating his sitting up in a chair.

On physical examination the patient appeared to be a well-developed and somewhat overweight man in no apparent distress. The peripheral arteries showed slight thickening. The pulse was regular at a rate of 85 and the blood pressure was 170 systolic and 90 diastolic. The heart was moderately enlarged to the left. The heart sounds were somewhat distant, and a systolic murmur could be heard at the apex transmitted to the axilla. There was no evidence of congestive failure. The right inguinal ring was markedly enlarged, and the right side of the scrotum was filled with a large reducible mass. The blood Wassermann test was negative.

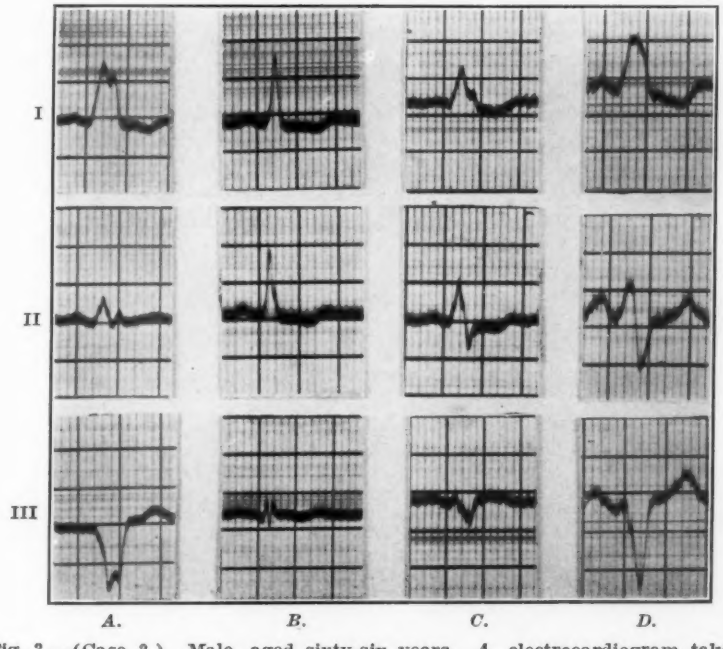

Fig. 3.—(Case 3.) Male, aged sixty-six years. *A*, electrocardiogram taken Aug. 8, 1933, showing typical left bundle-branch block. *B*, tracing taken Aug. 30, 1933, after bed rest, oxygen per nasal catheter, and complete digitalization. The bundle-branch block has entirely disappeared. *C*, electrocardiogram taken Sept. 23, 1933, three days after vasectomy had been performed. Left bundle-branch block has returned although the tracing differs in several respects from that taken on August 8. *D*, electrocardiogram taken April 20, 1934, on readmission to the hospital. Marked congestive failure present. Persistent bundle-branch block with evidences of progressive myocardial degeneration.

A diagnosis was made of right indirect inguinal hernia, coronary and hypertensive heart disease, moderate cardiac enlargement, relative mitral insufficiency, functional capacity Class IIA.

The inguinal hernia was repaired surgically July 15, 1933. On August 1 the patient complained of sharp pain in the lower left chest on deep inspiration. The skin was covered with a cold sweat, and the lips were cyanotic. A pleural friction rub could be heard over the lower left chest laterally. Both the pain and the friction rub lasted for three days. On August 6 he complained of a sharp pain in the lower right chest aggravated by inspiration. The pain was so severe on lying

down that the patient was forced to sit up all night. The respirations were shallow, rapid, and irregular. The pulse rate was 104. The skin was cool and very moist. The blood pressure was 185 systolic and 110 diastolic. Gallop rhythm was present at the apex. The liver was slightly enlarged, and there was pitting edema of both lower extremities. An electrocardiogram taken August 8 (Fig. 3*A*) showed a slight tachycardia and a typical left bundle-branch block. The P-R interval was 0.14 and the QRS 0.16 of a second. Oxygen was administered by nasal catheter and digitalization was started. The patient gradually improved, and on August 30 another electrocardiogram (Fig. 3*B*) was taken which showed no evidence of bundle-branch block although there were still definite signs of advanced myocardial changes. The S-T segments were depressed in Leads I and II, and the T-waves were diphasic in all leads. The P-R interval was 0.16 and the QRS 0.09 of a second.

A few days later the patient developed an epididymitis and was transferred to the genitourinary service for treatment. On Sept. 20, 1933, a left vasectomy was performed. Three days later the electrocardiogram was repeated (Fig. 3*C*) and showed a return of the bundle-branch block and decreased amplitude of the QRS complexes. The P-R interval was 0.13 and the QRS 0.14 of a second. He improved steadily and was discharged on Nov. 28, 1933.

On April 18, 1934, the patient was readmitted to the hospital complaining of weakness, shortness of breath, loss of appetite, and pain over the lower part of the abdomen. He frequently became so short of breath at night that he had to get up and sit in a chair. He had gained 35 pounds in weight during the preceding four months.

Physical examination revealed marked dyspnea and cyanosis, marked cardiac enlargement, and general anasarca. The electrocardiogram taken April 20, 1934 (Fig. 3*D*), showed a left bundle-branch block. The rhythm was regular at a rate of 100. The QRS complexes were somewhat changed in shape and amplitude as compared with the previous tracing (Fig. 3*C*), and the intraventricular conduction time was considerably lengthened. The P-R interval was 0.16 and the QRS 0.18 of a second. The patient was kept at complete rest, digitalized, and the fluid intake limited to 1,500 c.c. per day. He improved on this regime and was discharged on May 1, 1934.

Case 4.—N. P., a farmer, aged sixty-five years, was admitted to the Wisconsin General Hospital Dec. 28, 1933, complaining of shortness of breath. He had felt fairly well and had been able to do his farm work until August 29, when he had a sudden attack of "indigestion" accompanied by loss of taste and marked dryness of the mouth. On recovery from this attack he noticed that he was very short of breath, particularly on exertion. He coughed a great deal, especially in the morning, and raised large amounts of sputum. Both the cough and the shortness of breath had become gradually worse until just before his admission to the hospital, when he was able to do only a few minor chores on the farm. There had been a loss of 20 pounds of weight during the past four years. The family history was significant in that both parents had died of heart disease.

Physical examination revealed a rather small, elderly man, who had obviously been losing weight. Ophthalmoscopic examination revealed moderate sclerosis of the retinal arteries and definite engorgement of the retinal veins. The radial and brachial arteries were markedly sclerotic. The blood pressure was 170 systolic and 100 diastolic. There was slight enlargement of the heart to the left. The heart sounds were distant, and no murmurs were heard. Many crepitant, wheezing and sibilant râles were heard throughout both lungs, more marked at the bases. The liver edge was palpable 2 cm. below the right costal margin.

The blood Wassermann test was negative, and the sputum was repeatedly negative for tubercle bacilli. Lipiodol insufflation of the lungs showed definite bronchiectatic

dilatation in both lower lobes. An electrocardiogram taken Jan. 2, 1934, showed a normal sinus rhythm at a rate of 85 with one ventricular premature contraction following each normal beat. The QRS complexes were of low voltage in all leads and slightly slurred in Leads I and III. The P-R interval was 0.16 and the QRS 0.09 of a second. This tracing was interpreted as consistent with rather advanced degenerative changes in the myocardium, but indicated no extensive interference with the conduction mechanism.

A diagnosis was made of bronchiectasis, emphysema, coronary and hypertensive heart disease with slight cardiac enlargement, myocardial degeneration, dilatation of the aorta, extrasystolic arrhythmia, and lowered cardiac reserve, Class IIA. He was discharged from the hospital Feb. 3, 1934.

On Nov. 16, 1934, the patient was readmitted complaining of progressive weakness and increasing shortness of breath. Recently he had noted swelling of the ankles when up and around. The cough had persisted.

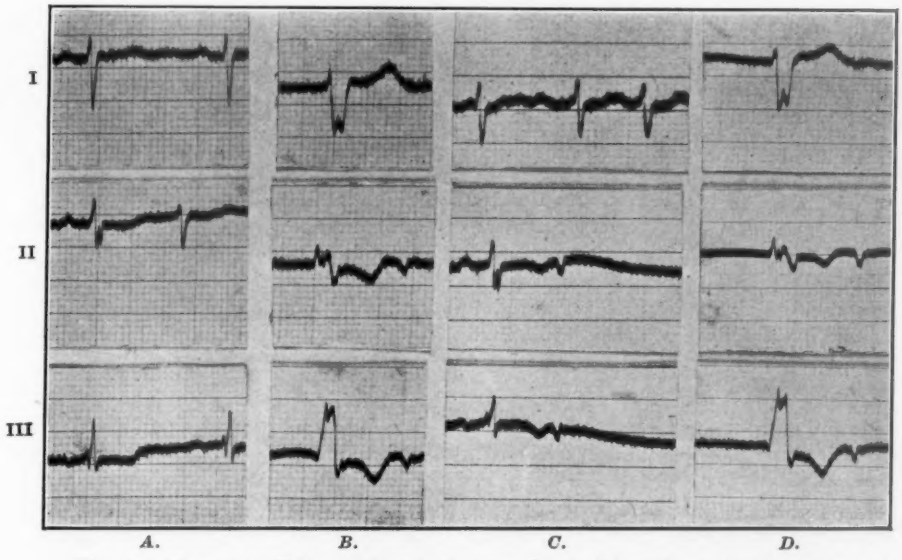

Fig. 4.—(Case 4.) Male, aged sixty-five years. *A*, taken Nov. 26, 1934. Normal rhythm is interrupted by periods of bigeminal rhythm, the second beat of the couplet apparently being an ectopic beat arising close to the A-V node. Right axis deviation but no evidence of bundle-branch block. *B*, taken Dec. 12, 1934, showing typical right bundle-branch block. Patient at bed rest and receiving maintenance dose of thevetin. Note inverted P-wave following the T-wave in Leads II and III. *C*, taken Dec. 17, 1934. No change in treatment. Lead I shows paroxysmal auricular fibrillation. Bundle-branch block has disappeared. *D*, taken Dec. 29. 1934, when patient was obviously failing. Right bundle-branch block has recurred.

On physical examination he was obviously dyspneic, and the lips and fingers were cyanotic. The blood pressure was 128 systolic and 100 diastolic. A positive centrifugal venous pulse was present. The heart sounds were distant, and no murmurs were heard. Frequent extrasystoles were noted on auscultation. The liver was palpable 4 cm. below the right costal margin. Numerous moist râles were heard throughout both lungs. Moderate pitting edema was present in the lower extremities. The diagnosis was the same as on the first admission except that the heart disease had become the primary factor, and the functional capacity was regarded as Class III.

The patient was put at complete bed rest and treated for congestive failure, oxygen being administered continuously by nasal catheter. An electrocardiogram

taken November 19 (Fig. 6*A*) showed in Lead I an apparently normal sinus mechanism with right axis deviation changing to a right bundle-branch block and at the same time a shift of the pacemaker to a point in the neighborhood of the A-V node. The onset of the bundle-branch block was preceded by a QRS complex apparently of a transitional type. One week later, on November 26, the electrocardiogram (Fig. 4*A*) showed periods of normal rhythm alternating with periods in which each normal beat was followed by a premature contraction apparently arising close to the A-V node. There was right axis deviation but no evidence of block. The P-R interval was 0.17 and the QRS 0.09 of a second. Oxygen was discontinued on December 1, and the next electrocardiogram, taken December 12 (Fig. 4*B*), showed a typical right bundle-branch block and a regular rhythm in which the pacemaker was situated in or below the A-V node as the P-waves were inverted and followed closely after the T-waves. The QRS interval was 0.16 of a second. For a short time the general condition appeared to improve slightly from day to day and on December 17 the electrocardiogram (Fig. 4*C*) showed an absence of the bundle-branch block. A short paroxysm of auricular fibrillation was recorded in the first lead but in Leads II and III there was a definite bradycardia and a blocked ectopic auricular rhythm which had been noted on a previous occasion. The P-R interval was 0.17 and the QRS 0.10 of a second. A few days later, the family, who were aware of the poor prognosis, expressed the desire to have the patient return home, and on December 21 an attempt was made to get him dressed for the trip, but the exertion produced such marked dyspnea that the idea had to be abandoned. The patient lost ground steadily, and on December 26 he complained of a severe pain over the precordium which lasted for several hours. On the following day a pleuro-pericardial friction rub was noted close to the left cardiac border. An electrocardiogram taken December 29 (Fig. 4*D*) showed a return of the right bundle-branch block, and the same rhythm as noted on December 17 (Fig. 4*C*). From this point on the clinical course was progressively downhill and the patient expired Jan. 5, 1935.

Necropsy was performed six hours post mortem and the most important findings were in the lungs and heart. The lungs showed marked emphysema and a congenital type of bronchiectasis. The heart weighed 430 gm. The left coronary artery was somewhat tortuous, with a small amount of thickening and slight longitudinal furrowing. The myocardium was rather pale with small areas of raised scarring. The aortic cusp of the mitral valve was thickened and contained a small area of calcification. Microscopic examination of the myocardium showed hypertrophy, marked diffuse fibrosis, some lipomatosis, moderate vacuolization and hyaline degeneration of the muscle fibers. The lungs, liver, spleen, and kidneys all showed marked chronic passive congestion.

CASE 5.—Mrs. J. B., aged fifty-six years, was admitted to the Wisconsin General Hospital, March 13, 1931, with a chief complaint of pain in the abdomen. There had been no symptoms referable to the heart. The past history included rheumatic fever, several attacks of pleurisy, and cholecystectomy in 1929.

On physical examination the pulse was regular at a rate of 90. The blood pressure was 128 systolic and 92 diastolic. The peripheral arteries were slightly sclerotic. The heart was slightly enlarged to the left. The heart sounds were normal at all areas; no murmurs were heard; and there were no signs of congestive failure. A diagnosis was made of peptic ulcer and postoperative abdominal adhesions.

The day following admission the patient experienced an attack of severe vomiting, the vomitus containing a small amount of blood. She was placed on routine treatment for acute gastric ulcer and gradually improved. On April 10, 1931, she ex-

perienced a second attack accompanied by upper abdominal pain of such severity as to be controlled with difficulty by morphine. Gradual improvement followed this attack and on April 15 an electrocardiogram (Fig. 5*A*) showed normal rhythm, rate 100, left axis deviation, S_1 and S_3 widened and slurred. The S-T segment was slightly depressed in Leads I and II, with upward convexity in Lead II but practically isoelectric in Lead III. T_2 was slightly inverted and T_3 was sharply inverted. The P-R interval was 0.16 sec., and the QRS 0.14 sec. Because of the electrocardiographic findings it was felt that the recent attack might have been of coronary origin. An electrocardiogram taken May 22, 1931 (Fig. 5*B*), showed an upright T_2 and T_3 with the P-R and QRS intervals within normal limits. The patient was discharged May 26, 1931, very much improved.

On Feb. 27, 1934, the patient was readmitted for a pelvic operation. At this time she complained of some dyspnea on exertion. The physical examination was

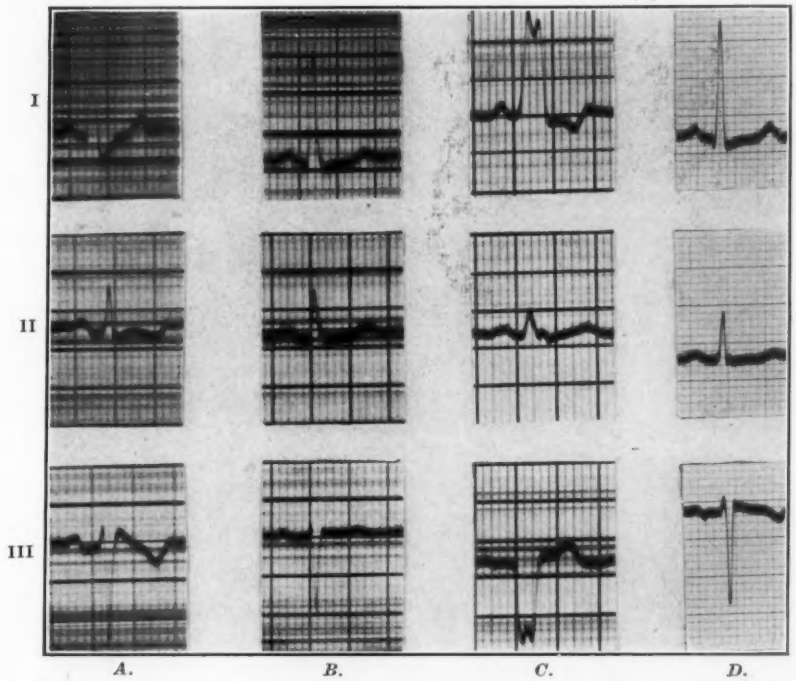

Fig. 5.—(Case 5.) Female, aged fifty-six years. *A*, electrocardiogram taken April 15, 1931, five days after an attack which may have been a coronary occlusion. No evidence of bundle-branch block. *B*, electrocardiogram taken May 22, 1931. Changes in T_2 and T_3 consistent with previous coronary occlusion. *C*, electrocardiogram taken March 1, 1934, showing definite left bundle-branch block. *D*, electrocardiogram taken Jan. 18, 1935. Bundle-branch block has disappeared.

essentially the same except that the blood pressure was found to be 180 systolic and 100 diastolic. A diagnosis was made of rheumatic and hypertensive heart disease, slight cardiac enlargement, functional capacity, Class IIA. An electrocardiogram taken March 1, 1934 (Fig. 5*C*), showed a definite left bundle-branch block. An operation for perineal repair was performed March 5, 1934, and the patient made an uneventful recovery, being discharged from the hospital March 30, 1934.

The patient was admitted for the third time Jan. 4, 1935, for the treatment of a ventral hernia which had developed in the wound of an old abdominal incision. The physical examination was essentially the same as on the previous admissions.

The blood pressure was 170 systolic and 108 diastolic. An electrocardiogram taken Jan. 18, 1935 (Fig. 5*D*) showed the bundle-branch block to have disappeared although the S-T segment still showed slight deviation in Leads I and III. The patient was fitted with a belt for the support of the ventral hernia and discharged Jan. 24, 1935.

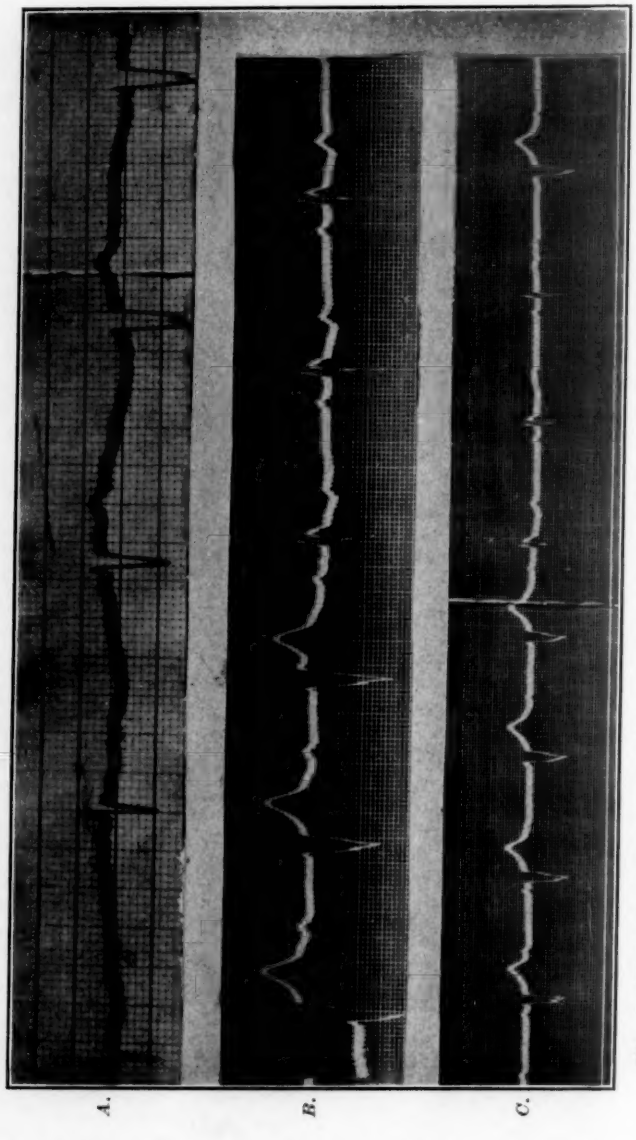

Fig. 6.—Three instances of transition to and from bundle-branch block. *A*, Case 4. Lead I taken Nov. 19, 1934. *B*, Case 6, female aged fifty-four years, coronary sclerosis, Lead III taken June 12, 1935. *C*, Case 6, Lead III taken June 14, 1935.

*CASE 6.—Mrs. D. R., a woman aged fifty-four years, was admitted to the Madison General Hospital on June 11, 1935, with a chief complaint of shortness of breath. The patient stated that for the past four years she had had attacks of what she termed "asthma" which had been increasing in frequency and severity

*Case included with the kind permission of Dr. J. S. Supernaw, Madison, Wis.

recently. She was unable to lie down during the attacks, and they were usually followed by a period of weakness lasting for one or more days. Except for occasional palpitation she had no other symptoms referable to the heart although she had been known to have "heart trouble" for several years. The past history included a tumor of the right breast with radical amputation six years previously and a removal of a tumor from the right axilla two years later. Cholecystectomy and appendectomy had been performed some years before.

On physical examination the pulse was found to be regular at a rate of 54, and the blood pressure was 238 systolic and 104 diastolic. Marked dyspnea was present. The right breast had been removed. The heart was enlarged to the left, and there was a systolic murmur at the apex, transmitted to the axilla. A systolic murmur was audible also at the aortic area. The lungs were clear, and there was no edema of the extremities.

An electrocardiogram taken on June 12 (Fig. 6*B*) showed complete heart-block alternating with periods of 2:1 A-V block, the auricular rate varying between 85 and 90 and the ventricular rate between 43 and 45. Left bundle-branch block was present in Leads I and II but disappeared during the taking of Lead III, the transition having been recorded. The QRS complexes were widened and slurred in all leads, the QRS interval being 0.15 of a second. T_1 was inverted. An electrocardiogram taken June 14, 1935 (Fig. 6*C*), was similar to the one taken two days previously, and again a transition period was recorded in Lead III. The patient remained in the hospital under observation for six weeks, during which time it was found that the attacks responded promptly to 1/100 of a grain of nitroglycerin. Rather large doses of barbiturates and frequently repeated doses of nitroglycerin kept her fairly free from attacks of dyspnea. She was discharged very much improved Aug. 6, 1935.

DISCUSSION

All of the patients here reported were above fifty-four years of age and at a period of life when coronary disease and degenerative changes are known to be extremely prevalent. Coronary sclerosis, hypertension, or a combination of the two, was demonstrable in each instance. In Cases 1 and 5 there was no apparent change in the clinical condition between the time that the bundle-branch block was first discovered and the time it was found to have disappeared, but in the other four cases there seemed to be a definite relationship between the presence of the bundle-branch block and the condition of the circulation in general. This was most graphically illustrated in Case 2 in which the bundle-branch block was present directly following a coronary thrombosis but disappeared during the period of recovery and the establishment of collateral circulation. The period during which this patient was under observation was marked by steady and gradual improvement, and no recurrence of the bundle-branch block was noted. In Cases 3 and 4 the bundle-branch block appeared and reappeared during periods of decompensation and persisted as long as signs of circulatory failure were in evidence but disappeared when compensation was restored. When the condition of the myocardium reached a point where congestive failure could no longer be overcome, the bundle-branch block became permanent.

The explanation of the mechanism is simple, as it appears to be plainly a matter of circulation and nutrition to the conducting tissues. When the myocardium was failing and the general circulation was obviously inadequate, it was reflected in the coronary circulation by the appearance of bundle-branch block and other conduction disturbances. As the general circulation improved under treatment, the blood supply to the myocardium and conduction system became sufficient to permit the transmission of the impulse along the normal pathways. Widespread damage throughout the myocardium, as was demonstrated at necropsy in Case 4, is undoubtedly an important contributing cause, and in the presence of such a condition a temporary decrease in the efficiency of the coronary circulation is the deciding factor in the production of marked disturbances in the conduction mechanism.

It was an interesting circumstance that the one case which exhibited right bundle-branch block showed a right axis deviation in the records in which the bundle-branch block was absent, and similarly, the five cases in which there was a transient left bundle-branch block showed either a left axis or a tendency to left axis deviation in the "normal" records.

Willius and Anderson remarked that transient bundle-branch block is probably more common than the number of reported cases would indicate, and this view is supported by the occurrence of these six cases in a relatively short space of time.

SUMMARY

Six cases of transient bundle-branch block are presented, three of which show one or more recurrences. All of the patients were above fifty-four years of age and in every instance organic heart disease was demonstrable, the etiology being coronary disease, hypertension, or a combination of the two. In two of the six cases the occurrence of the bundle-branch block was closely associated with periods of myocardial failure, and in one case was present for a time following coronary occlusion. In two instances no associated change was demonstrable in the general circulatory condition. One patient died and came to necropsy, and the other five are still living.

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THE INFLUENCE OF POSTURE ON PARTIAL HEART-BLOCK*

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IT HAS long been known that there is a heightened vagus effect in the reclining position as compared to the upright. Mosso[1] in 1884 attempted to explain the phenomenon, but physiologists even today, although recognizing its existence, are uncertain as to the cause. Its application to clinical medicine theoretically would be limited to conditions where the sympathetic-parasympathetic balance is so delicately adjusted that a slight added vagus effect would determine parasympathetic predominance. A case of partial heart-block was observed in a case in which just such a situation apparently existed, and its analysis suggests that the condition may not be infrequent.

CASE REPORT

A banker, sixty-four years of age, was first seen on April 28, 1935, with the *chief complaints* of "dizzy spells" accompanied by occasional vomiting, of one month's duration. The *family history* was irrelevant, as was the *past history* with the exception of an abscess on the left side of the neck near the angle of the jaw three years previously. This was excised and left a rather deep scar. The *present illness* began with a sudden attack of dizziness which lasted off and on for several hours. It was accompanied by nausea and vomiting. Similar attacks of varying duration occurred at irregular intervals, but none so severe or prolonged as the first. There was no apparent relation to time of day or to posture as attacks appeared both while he was lying down and while he was sitting. No attacks, however, were recalled as having occurred while he was standing. Since onset some palpitation and a feeling of irregular heartbeat occurred. There was no loss of consciousness at any time. The only medication had been 0.3 c.c. of tincture of strophanthus two days before admission.

Physical examination revealed a well-preserved man of sixty-four years. Other than a small deep scar in the neck just beneath the angle of the left mandible and a moderate amount of postural emphysema, the positive findings were limited to the cardiovascular system. The heartbeat was not visible, and there was no enlargement to percussion. The rate (patient supine) was 48, and the rhythm was grossly irregular. The sounds were faint but otherwise normal. The radial arteries and those of the eyegrounds were distinctly sclerosed. *Laboratory findings* were negative other than a roentgen ray film of the chest, which showed a slight enlargement of the heart to the left and a widened and much lengthened aorta.

A significant fact was that on examination of the heart when the patient was standing, the rate was 96 and the rhythm became apparently regular. Then in the supine position the rate immediately returned to 48 and the rhythm was irregular. The patient was placed under the fluoroscope on a tilt-top table. When he was supine, the rate was estimated at 36. The table was slowly tilted toward the vertical position, and, when it made an angle of approximately 70 degrees with the floor, the rate suddenly doubled and remained so as long as the table was no more hori-

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zontal than this. When the table was tilted back toward its original position, the rate again slowed. This process was repeated several times, and the phenomenon was observed consistently.

Electrocardiograms taken with the patient in various positions revealed a partial heart-block. With the patient supine the auricular rate was 62, the ventricular rate 35, giving a ratio of approximately 1.8:1. The P-R interval varied from 0.2 to 0.4 second (Fig. 1). With the patient sitting erect, the auricular rate remained about the same, but the ventricular beats increased to 43 per minute, a ratio of about 1.4:1 (Fig. 2). When the patient was standing, the auricular and the ventricular rates were 71 (Fig. 3).

The effect of exercise was tested. With the patient reclining and also before stepping upon a chair several times until dyspnea was pronounced, the auricular beats were 72 and the ventricular 53. Immediately after exercise with the patient supine the auricular rate was 80 and the ventricular rate 75, with the P-R interval prolonged (Fig. 4). With the patient standing, the auricular rate promptly rose to 92, with the ventricle responding to each impulse over an observation period of one minute (Fig. 5).

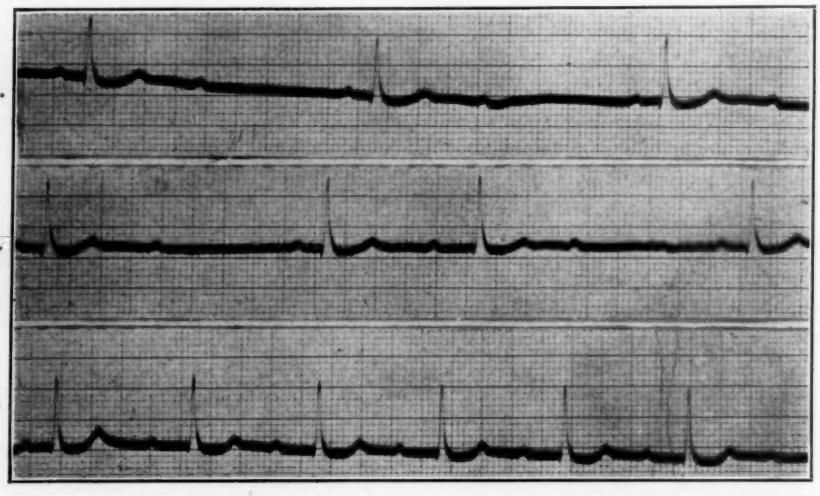

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1.—Patient supine: P-R interval, 0.2 to 0.4 sec.; auricular rate, 62; and ventricular rate, 35.5.

Fig. 2.—Patient sitting: auricular rate, 62; ventricular rate, 43; and P-R interval, 0.2 to 0.4 sec.

Fig. 3.—Patient standing: P-R interval, 0.28 sec.; auricular rate, 71; and ventricular rate, 71.

Atropine sulphate was shown to have a marked effect on the conduction mechanism. Before the administration of 0.0012 gm. subcutaneously, the auricular and the ventricular rates with the patient reclining were 60 and 45, with the P-R interval extending from 0.2 second to 0.34 second. Forty-five minutes after the administration of atropine the auricular and the ventricular rates were 80 with the patient supine, and the P-R interval became stabilized at 0.24 second (Fig. 6). The patient was then given 0.0006 gm. of atropine sulphate by mouth every eight hours. The conduction mechanism remained normal thereafter in all positions, although the P-R interval continued to be somewhat prolonged. This dose of atropine was continued after discharge from the hospital, with occasional omissions of one dose on days when dryness of the throat became excessive. No further symptoms occurred. On June 22, while the patient was still taking atropine, there was no abnormal alteration in rate with change of posture. The P-R interval was 0.22 second (Fig. 7).

DISCUSSION

When the vagus influence on the heart rate in the case here reported was first recognized, it was considered probable that there was mechanical pressure somewhere about the carotid sinus or vagus trunks. The symptoms in this case were not unlike those reported by Weiss[2] in patients in whom such mechanical factors had been discovered. This supposition seemed all the more probable because of the scar in the neck quite near the carotid sinus. However, digital pressure over that area as well as on the right side of the neck caused no pronounced slowing of the rate, regardless of the patient's position. The mediastinum, examined

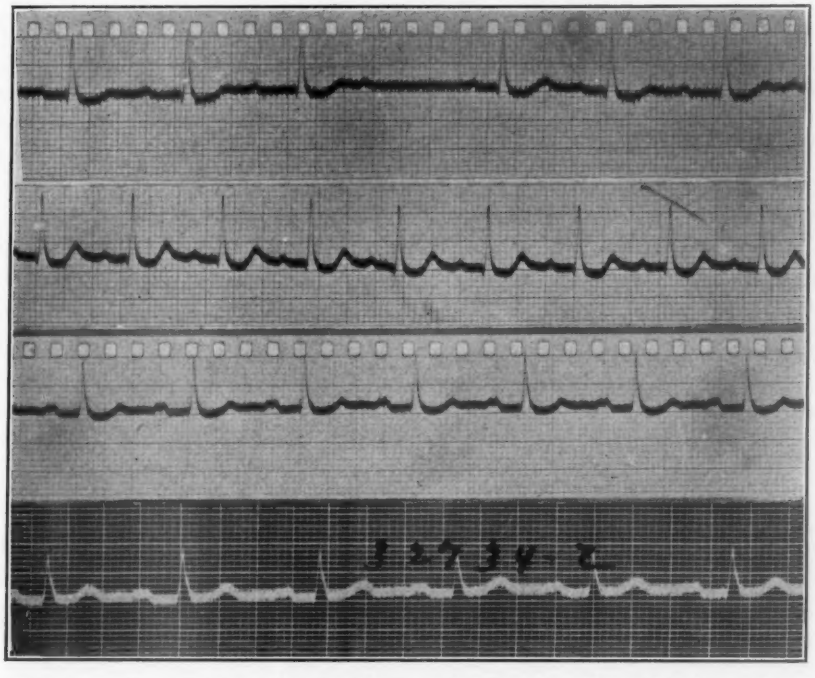

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 4.—Patient supine after exercise: auricular rate, 80; ventricular rate, 75; and P-R interval, 0.22 to 0.32 sec.

Fig. 5.—Patient standing after exercise: auricular rate, 92; ventricular rate, 92; and P-R interval, 0.2 sec.

Fig. 6.—Patient supine forty-five minutes after atropine sulphate (0.0012 gm. subcutaneously): auricular rate, 80; ventricular rate, 80; and P-R interval, 0.24 sec.

Fig. 7.—Patient sitting (after six weeks with atropine sulphate medication, 0.0006 gm. orally three times a day): P-R interval, 0.22 sec.; and rate, 84.

by a series of roentgen ray films taken at various angles, was found to be normal. Lipiodol instilled into the trachea showed no abnormality of the larger air passages. The normal contour of the esophagus was revealed under the fluoroscope after barium was swallowed.

In view of these negative findings it was believed that the case was one of early heart-block of organic etiology, as indicated by a consistently prolonged P-R interval. The disease had apparently progressed to the

point where the function of conduction was barely adequate to permit all auricular impulses to pass through the bundle of His while the patient was erect.

The slight vagus effect always present on reclining or sitting, superimposed upon the organic lesion, was sufficient to magnify the block greatly. The supposition that the slowing of the ventricular rate was vagal in origin was demonstrated by its correction with small doses of atropine.

The effect of posture on the heart rate apparently varies in different individuals. It is generally believed that the difference in rates observed in the lying and sitting positions is due to pressure effects on the carotid sinus. The further difference that occurs between the sitting and the standing positions is thought to be due to another mechanism as yet not agreed upon. MacWilliam[3] has recently discussed the problem and reviewed the relevant literature. In the above case it is not clear why pressure on the neck did not have a pronounced effect on the rate, when the effect of posture alone was so pronounced.

One other observation somewhat similar to that recorded here was made by Erlanger[4] in 1905. He described a patient with complete heart-block, in whom there was a rise in auricular rate only on assuming the upright position. Under antisyphilitic treatment there was gradual release of the block. When this had assumed the phase of a 3:1 ratio, both the auricle and the ventricle beat faster with the patient standing. Moderate exercise also brought about a proportionate increase in the rates of each ventricle when the block was both complete and partial. Severe exercise, however, caused partial heart-block to become more complete.

It is presumed that our patient was seen at a period during the progression of an organic heart-block in which the vagus influence now plays an important part. This rôle may become less as the lesion progresses. It is entirely possible that similar occurrences with heart-block are not infrequent.

SUMMARY

A patient with partial heart-block, presumably of organic nature, had a ventricular rate much faster in the upright position than when recumbent. It appears that this discrepancy is due to vagus effect. Under atropine medication the block (other than a prolonged P-R interval) and its attendant symptoms disappeared.

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HEART-BLOCK FOLLOWING X-RAY TREATMENT FOR THYROTOXICOSIS*

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THE present study involves observations made upon a case of toxic goiter in which x-ray therapy was followed by the development of transient heart-block. Prolongation of the auriculoventricular conduction time in the presence of hyperthyroidism, although seldom recognized, was found by Goodall and Rogers[8] in 242 of their 787 cases of goiter. Auriculoventricular dissociation, however, is very rare. In ten studies[1, 2, 5, 8, 10, 11, 14, 17, 20, 21] in which electrocardiograms were made in a total of 1,844 cases of hyperthyroidism, complete dissociation was noted in only five instances. Individual cases in which Adams-Stokes attacks occurred as a complication of thyrotoxicosis have been reported by Merklen,[13] Reilingh,[15] and Carey.[3] Incomplete block has been observed in two cases by Cameron and Hill[2] and in isolated cases by Lewis,[12] Simon[16] and Easton.[7] Complete block, confirmed by electrocardiogram, has been reported in two cases by Dameshek[5] and in six cases by Davis and Smith.[6]

Although the view that hyperthyroidism characteristically improves auriculoventricular conduction has been denied by Joll[9] on the basis of insufficient evidence, thyroid extract is nevertheless often used successfully in the treatment of Adams-Stokes attacks. Hyperthyroidism at least produces no apparent lesion to account for the occurrence of heart-block. Recent authors[2, 3, 6] have therefore attributed the arrhythmia under the circumstances to intercurrent infection, to underlying organic heart disease, or to digitalis intoxication. The present case is remarkable for the absence of these factors, and in the mode of onset of the block it is apparently without precedent in the literature.

CASE REPORT

E. D., a young Italian woman, twenty-five years old, was admitted to St. Agnes Hospital on May 29, 1935, complaining of fainting attacks. Four years previously, she had first noticed an enlargement of the base of her neck and a tendency to unusual dyspnea and cardiac palpitation on effort. Nine weeks before admission she attended the out-patient department of another hospital to inquire about the swelling of the neck, stating that she was not nervous, had lost no weight, and felt in general quite well. On physical examination at that time, the only significant abnormalities were a goiter of moderate size, over which a bruit could be heard, slight exophthalmos, a coarse tremor of the hands, small but infected tonsils, and a soft systolic murmur at the cardiac apex. Five weeks later a metabolic rate test

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was reported as 40 per cent; on repetition a month later it was 25 per cent. The following week, however, a loss of five pounds in weight was considered indication for x-ray therapy, which was applied (200 volts, 8 milliamperes) for 18.2 seconds on May 6, and this was repeated on May 13. There was no significant reaction

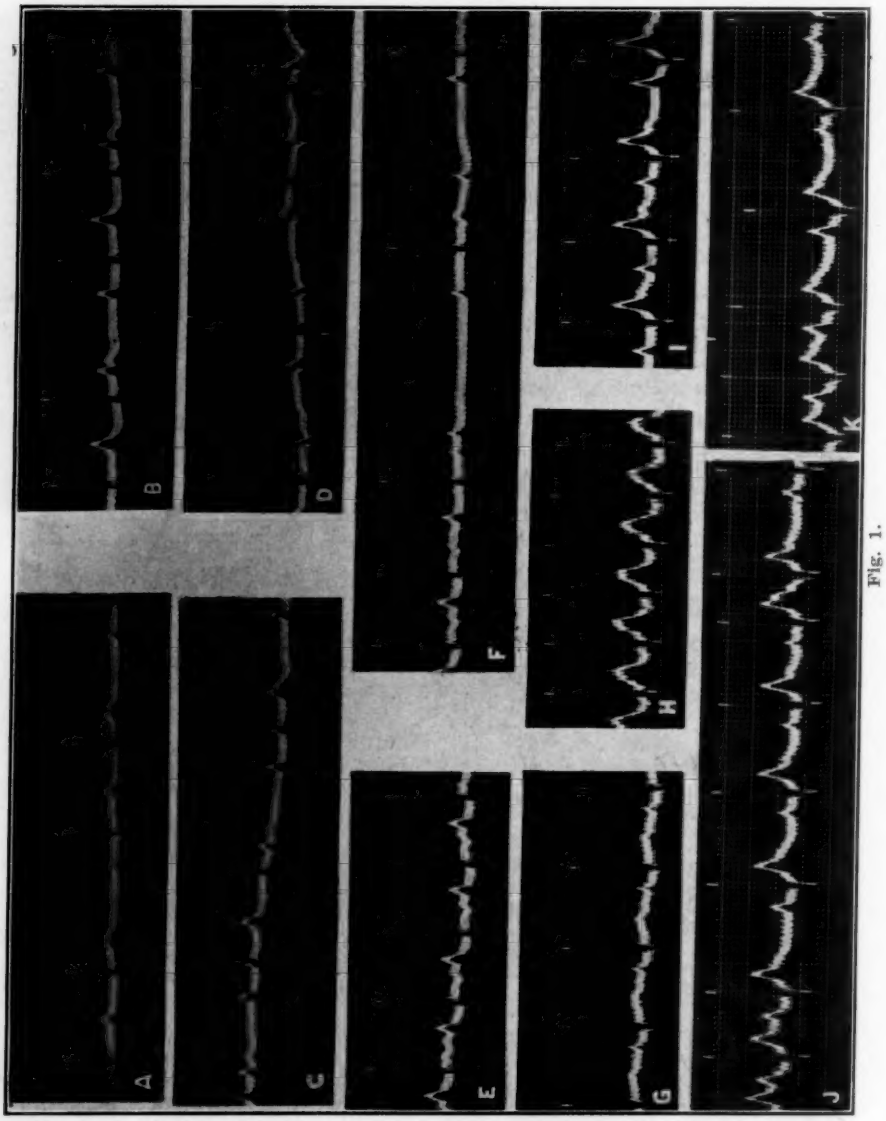

Fig. 1.

Fig. 1.—*A, B, C, D:* Leads I, II, III, and IV, respectively, of electrocardiogram showing 3:2 and 2:1 heart-block.

E, two days later, reversion to normal sinus rhythm with P-R intervals of 0.20 to 0.22 second (Lead II).

F, same, showing block produced by carotid sinus pressure.

G, eight days later, P-R intervals 0.16 second (Lead II).

H, same, tachycardia three minutes after adrenalin.

I, same, slowing of heart rate six minutes after adrenalin (P-R intervals 0.22 second).

J, same, sino-auricular block, nine minutes after the adrenalin injection.

K, same, bradycardia produced by carotid sinus pressure.

during treatment, but following the first application the patient "felt badly" and complained of pain in the thyroid region. After the second treatment these symptoms became worse, and two days later, on returning home from a visit to the nose and throat clinic, she became nauseated and fainted. Her temperature was subnormal; the pulse was slow and "jerky." She improved during ten days in bed but on getting up she was again subject to repeated fainting attacks for which she was brought two days later to St. Agnes Hospital.

The past medical history was negative for rheumatic infections. She had had measles, whooping cough, influenza, and many colds, but very few attacks of tonsillitis and no recent respiratory infections. The family and social histories were irrelevant.

Physical examination showed a pale, rather nervous girl weighing 109 pounds, with no dyspnea or cyanosis. There was slight exophthalmos and a positive von Graefe sign. The tonsils were cryptic and infected, but there was no acute pharyngitis. The teeth were in fair condition. Situated deep in the neck was a small nodular goiter about the size of a hazelnut, involving the right lobe of the thyroid, which was readily observed on swallowing with the head held in hyperextension. Pulsation of the carotid vessels was marked, but the jugular pulsations were disproportionately rapid. The lungs were clear. The heart was apparently normal in size, and there were no thrills, but the precordial pulsation was violent and diffuse. The rate was irregular, averaging between 40 and 60 per minute. The heart sounds were loud and booming but of good quality. At the apex a soft blowing systolic murmur was audible, transmitted to the base. The abdomen was normal. There was no ankle edema, but the hands presented a coarse tremor. The radial pulse was full with no deficit. The blood pressure was 100/70.

Laboratory examination showed a negative Wassermann reaction and a normal blood chemistry. Urinalysis gave a specific gravity of 1.029, a cloud of albumin, and a few hyaline casts and white cells. The blood count was hemoglobin, 67 per cent; R.B.C., 3,460,000; W.B.C., 7,400; neutrophiles, 64 per cent; and lymphocytes, 36 per cent. The sedimentation rate was increased to 25 mm. per minute. Fluoroscopic examination showed the heart normal in size and contour. The metabolic rate test made three days after admission showed + 11 per cent. The electrocardiogram also made three days after admission showed an alternating 3:2 and 2:1 heart-block, the auricular rate averaging 110 and the ventricular rate 75. With the exception of a tendency to flattening of the T-waves in all leads there were no other significant abnormalities.

For the first five days the patient received Lugol's solution, three minims three times a day. The pulse rate increased from 40 to 80 by the fifth day, when medication was stopped to see if the block, which had disappeared, would return. The electrocardiogram now showed a normal sinus rhythm with a rate of 120 and rather prolonged P-R intervals of 0.20 to 0.22 second. On the eleventh day the P-R intervals were 0.16 second and the heart rate was 100. The T-waves in Leads I and II had definitely increased in amplitude. Examination of the heart showed no abnormalities other than the soft apical systolic murmur. Further convalescence was uneventful. The tonsils were removed without untoward effect. The patient was discharged in good condition on June 23, 1935, twenty-six days after admission, and since that time has had no abnormal cardiac signs or symptoms.

OBSERVATIONS

On admission the ventricular rate was much slower than when the first electrocardiogram was made three days later, and it is probable that at the onset of the arrhythmia there was a complete auriculo-

ventricular dissociation. On the fifth day when the second electrocardiogram was made, the block had disappeared except for prolongation of the P-R intervals which averaged from 0.20 to 0.22 second. At this time pressure applied to the carotid sinus produced a further prolongation of the P-R intervals to 0.28 second, followed by a 2:1 block. The auricular rate slowed from 115 to 70 and the ventricular rate to 35.

On the tenth day when the electrocardiogram appeared relatively normal and the P-R intervals measured 0.16 second, the effect of adrenalin was observed. With the patient seated, 1 c.c. of a 1:1,000 solution of adrenalin was given intramuscularly. The resting blood pressure was 114/75, and the pulse rate was 100. Within three minutes the blood pressure had increased to 160/90 and the pulse rate to 180. The electrocardiogram showed a sinus tachycardia with great increase in the height of the T-waves. At six minutes the rhythm became quite irregular due to transient periods of slowing of the heart rate to 100 accompanied by prolongation of the P-R intervals to 0.22 second. At eight minutes the P-R intervals had shortened to 0.16 second. At nine minutes the rhythm was interrupted by periods of sino-auricular block in which the rate slowed from 140 to 70 with occasional escapement of isolated beats. At fourteen minutes the heart rate had returned to 140, and the block had disappeared. Pressure on the carotid sinus now produced slowing of the rate to 100 but no change in the auriculoventricular conduction time.

During this period of observation, the patient was not seriously uncomfortable and complained only of severe palpitation. She stated that the sensation was similar to that experienced after x-ray treatment of the thyroid and before the onset of syncope. Auscultation of the heart exhibited the loud booming sounds of hyperdynamic action but aside from the systolic murmur previously noted, no other abnormalities were apparent.

DISCUSSION

The cause of the heart-block in this case is not at once apparent. Since the action of digitalis can be excluded, there remain four agencies by which it might have been produced: systemic infection, organic heart disease, thyrotoxicosis, and hyperactivity of the vagus. There was, however, no evidence of infection. The patient exhibited no cough, fever, pharyngitis, or leucocytosis. Tonsillectomy failed to cause a recurrence of the arrhythmia. Likewise organic heart disease can probably be excluded in the absence of a history of rheumatism or the appearance of definite clinical signs. Thyrotoxicosis would seem to be the most likely explanation but for the fact that heart-block is exceedingly rare in this condition and is almost always explainable on the basis of other factors. Furthermore, the patient was not very "toxic"; the basal metabolic rate was only +11 per cent, and the mani-

festations of hyperthyroidism were relatively mild. One is led to assume therefore that an abnormal vagal effect was the factor primarily responsible for the arrhythmia.

Hyperactivity of the vagus as an explanation of the occurrence of heart-block in the present case is supported by the fact that the vagus is now generally recognized as a frequent contributory factor in heart-block[4] and occasionally appears to be its sole mechanism.[19] Simon[16] attributed the occurrence of heart-block in his case to vagal damage sustained during thyroidectomy. A vagus effect is indicated in the present case by the fact that auriculoventricular dissociation could be reproduced by carotid sinus pressure in the initial period following the return of sinus rhythm.

The question arises as to the manner in which the vagus was affected. That stimulation was not due to pressure of the enlarged gland on the nerve trunk is certain from the absence of substernal goiter and the fact that digital compression of the gland failed to evoke any change in heart rate. Nor was any significant response elicited by swallowing or by ocular pressure. The logical conclusion is that excitation of the vagus was by way of the carotid sinus.

At the time when the P-R intervals were still prolonged, auriculoventricular dissociation could be produced by pressure on the carotid sinus. Later when the P-R intervals had become normal in duration, this procedure was without effect except for the characteristic slowing of the heart rate. Adrenalin was likewise ineffective in producing a recurrence of the block, except for a slight lengthening of the P-R intervals during the height of the rise in blood pressure. It appears, therefore, that the state of hyperactivity of the carotid sinus was a transient phenomenon. The only apparent cause was the x-ray therapy which it immediately followed and to which the carotid sinus was topically exposed. In other words, the carotid sinus, involved in the local application of x-rays to the thyroid, underwent a period of hypersensitivity which produced relative slowing of the heart rate at a time when the exacerbation of hyperthyroidism was at its height (auricular rate 110 in the first electrocardiogram as compared with 120 when the block had disappeared) and resulted in temporary auriculoventricular block.

The influence of the hyperthyroidism itself in the production of the block is uncertain. The frequently prolonged P-R intervals observed by Goodall and Rogers[8] have not been noted by other authors, and they themselves found no actual dissociation. In the present case, the mildness of the thyroid symptoms and the fact that there is no known mechanism by which hyperthyroidism can produce heart-block seem adequate bases for the belief that the rôle of the thyroid was negligible.

Whether or not the sino-auricular block was in any manner related to the hyperthyroidism is likewise problematical. Sino-auricular block

is not uncommon in young people and is often produced by adrenalin or vagal stimulation so that its occurrence under the circumstances is probably not remarkable. Attention in passing is merited, however, by the recognition of heart-block as a possible concomitant of hyperthyroidism. Without an electrocardiogram the arrhythmia may easily be interpreted as a bradycardia, for which reason the correct diagnosis of hyperthyroidism may be overlooked.

SUMMARY AND CONCLUSIONS

1. A case is described in which transient heart-block with Adams-Stokes syndrome occurred following x-ray therapy for toxic goiter.

2. Soon after restoration of normal sinus rhythm, auriculoventricular dissociation could be brought on by pressure on the carotid sinus. Later both carotid sinus pressure and the injection of adrenalin were ineffective in reproducing the block although adrenalin still caused transient prolongation of the auriculoventricular conduction time.

3. On the basis of the evidence at hand it was concluded that the heart-block was caused by hypersensitivity of the carotid sinus resulting from exposure to x-rays.

4. Attention is called to the clinical value of recognizing heart-block as a possible cause of bradycardia in the presence of hyperthyroidism.

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269 SOUTH NINETEENTH STREET

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Department of Clinical Reports

PRIMARY TUMOR OF THE HEART

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TUMORS of the heart, both secondary and primary, are not often reported in the medical literature. The highly differentiated and specialized myocardium, however, sometimes is the seat of secondary tumors and occasionally of primary neoplastic growth. Secondary tumors, compared with primary tumors, are found in the proportion of 16 to 1. There are approximately one hundred fifty-five cases of primary tumor of the heart reported; of these about forty-five are classed as sarcomas. The literature on this subject was extensively reviewed by Perlstein[1] in 1918, and by Goldstein[2] in 1922. Since then only a few isolated cases have found their way into the literature. Most primary tumors are essentially not malignant, falling into the classification of fibromas, myxomas, lipomas, and rhabdomyomas. The following is a report of a histologically typical rhabdomyosarcoma.

REPORT OF A CASE

M. W., female, sixteen years old, was first seen on April 18, 1933, when she complained of shortness of breath and extremely rapid pulse. She appeared apprehensive; her pulse was rapid, 140 per minute, temperature, 98.8° F.; and respirations, 36 per minute. The heart beats were difficult to obtain with a stethoscope, the sounds appearing quite distant. The abdomen was rigid in the upper portion and the liver was depressed three fingerbreadths below the costal margin.

History of Present Illness.—Six days prior to entry to the hospital, the patient complained of diffuse pains in her abdomen and marked fatigue. On the day of entry she complained of some dyspnea which became progressively worse. She was taken to the hospital that night in extremis.

Family history was essentially negative. Past History: The child was healthy up until twelve months before the onset of the present illness. She had been rather athletic and enjoyed ordinary outdoor exercise. One year before the onset of the present illness the mother noticed that the child began to complain of feeling fatigued on any strenuous exercise, which prior to this time had been enjoyed. The family thought that it was probably laziness on the girl's part and would scold her for not taking a greater share in the housework. Her disposition up until this period had been very smooth, quiet and peaceful, but at times she would become rather indignant when the family insisted that she do certain tasks about the house.

Course in the Hospital.—The patient presented moist râles throughout both lungs, anteriorly and posteriorly. A diagnosis was made on entry of fulminating bronchopneumonia with cardiac failure. Adrenalin was given, together with morphine and atropine. This was followed by caffeine and digalen stimulation. Oxygen

inhalations apparently gave some relief to the patient, but she failed to respond to therapy and died one hour and fifteen minutes after hospital entry.

Autopsy Report.—The body was that of a sixteen-year-old female appearing in a good state of nutrition. The skin generally had an especially marked florid appearance. The hair was abundant, abdomen distended, and extremities negative.

Fig. 1.—Illustration of heart showing tumor grossly confined to the auricles. The dark area is the point of gradual erosion and rupture of the auricular wall resulting in fatal hemorrhage. Because of this mass the auricle is almost entirely replaced by a solid tumor. Surface areas are nodular and friable and infiltrated by blood.

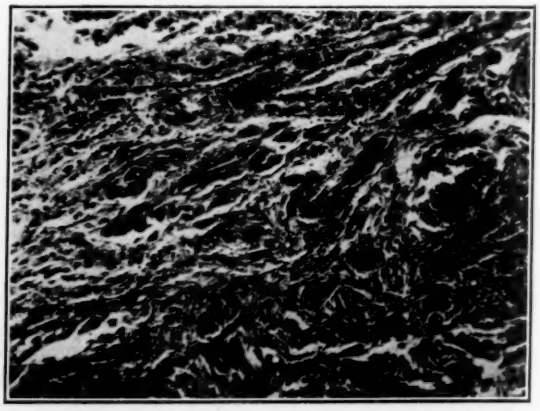

Fig. 2.—Low power picture of the tumor mass. Note the variation in size and shape of the cells with embryonic, immature characteristics. Resemblance to normal heart muscle fibers is well seen in some areas.

Upon opening the pleural cavities approximately 200 c.c. of serosanguineous fluid was found on each side. The heart had been pushed upward and backward by the tumor growth involving both auricles. Almost the entire area of both auricles was replaced by a nodular tumor growth, soft in consistency, somewhat friable, and markedly hemorrhagic. The auricular cavities were nearly filled by

the neoplastic process. Rupture had occurred in the region of the posterior aspect of the left ventricle, causing bleeding into the pericardial cavity. The pulmonary and aortic valves were not involved. Both the mitral and tricuspid valve rings were dilated, but smooth, and the valves themselves were not unusual. The weight of the heart was 880 gm.

The microscopic sections revealed an embryonic type of cell, small and fat spindle cells predominating. The cells were deep staining and showed mitoses. Giant cells were fairly numerous. There was some infiltration of both fresh red blood and old changed blood between the fibers, which gave the Prussian blue reaction for iron. There was microscopic invasion of the ventricular walls by the infiltrating tumor.

Both lungs were a beefy red in color and showed marked congestion. The microscopic sections revealed acute pulmonary edema with some passive congestion. Heart failure cells were in evidence showing a fairly long-standing process.

Liver: The liver was enlarged, firm in consistency and weighed 1700 gm. Cut section revealed a typical nutmeg appearance with marked bile stasis.

Pancreas: The pancreas was firm and somewhat fibrous and revealed on section a mild interstitial fibrosis.

The remaining organs and tissues apart from congestion revealed nothing noteworthy.

Diagnosis.—Primary rhabdomyosarcoma of the heart with rupture.

DISCUSSION

The tumor, although malignant, was confined to the heart. Like other reported cases of primary tumor of the heart, the site of origin was probably in the auricles. The ventricle walls on both sides showed microscopic infiltration but grossly appeared uninvolved. Death occurred from erosion of the left auricular wall with fatal exsanguination. This apparently was a slow erosion, with hemorrhage into the walls of the auricle as shown by the stasis of blood between the tumor fibers. Some of the spindle cells which appeared to be less embryonic showed areas of cross-striation. Mitoses were present, and giant cells were fairly common. Diligent search failed to reveal any evidence of tumor elsewhere in the body. This case, like the other reported cases we were able to study in the literature, was not diagnosed clinically before death.

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ELECTROCARDIOGRAPHIC CHANGES IN A CASE OF ELECTRIC SHOCK*

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THE following case is reported because of interesting electrocardiographic changes which occurred in rapid succession following electric shock. The changes occurred without clinically detectable structural cardiac disease or myocardial insufficiency.

CASE REPORT

W. C., white male motorman, thirty-six years old, was admitted to the Coney Island Hospital on the surgical service of Dr. Earl J. Miles† on Sept. 17, 1934. His family history was negative. His past history was likewise negative except for an electric burn in 1920.

While coupling two cars at about 6:00 A.M. on Sept. 17, 1934, he received a sudden electric shock which rendered him unconscious for about two minutes. He was admitted to the hospital shortly thereafter. Examination showed a well-developed young male, who did not appear ill. His respirations were normal. There was no cyanosis. The head and neck showed nothing abnormal. The heart was normal in size; the rhythm was totally irregular; and the sounds were of good quality. No murmurs were heard. The lungs were clear, and the abdomen was negative. Both lower extremities showed rather extensive second-degree burns.

The total irregularity of the heart which he showed on admission persisted for about three hours, and then there was a return to the normal sinus rhythm which continued throughout his stay in the hospital. At no time did he show any changes in the heart sounds, any signs of cardiac enlargement, or the slightest suggestion of myocardial insufficiency. His temperature was normal throughout with the exception of an occasional rise to 100° F., which could be attributed to inflammatory reaction and absorption from the burns of the extremities. The laboratory findings including blood chemistry, blood Wassermann reaction, blood count, urinalysis, and x-ray findings were negative. He was discharged on Oct. 15, 1934, in a perfectly normal condition.

Electrocardiographic Findings.—An electrocardiogram (Fig. 1) was taken at 8:30 A.M., shortly after his admission to the hospital. It showed auricular fibrillation with a ventricular rate of about 110 and a tendency toward left axis deviation. At 12 noon the same day there was regular sinus rhythm with auricular and ventricular rates of about 75 per minute (Fig. 2). The P-R conduction time was about 0.16 sec. The QRS complex in Lead I was of comparatively low voltage while that of Lead III was of higher voltage than in the previous tracing.

At 9:00 A.M. the following day the P-R conduction time was increased to 0.20 sec.; the QRS complexes were of much higher voltage; and there was a marked degree of left axis deviation (Fig. 3). Lead I showed slight depression of the R-T segment and a negative T-wave, while in Lead III the T-wave was positive with slight elevation of the S-T segment. The P-wave was markedly negative

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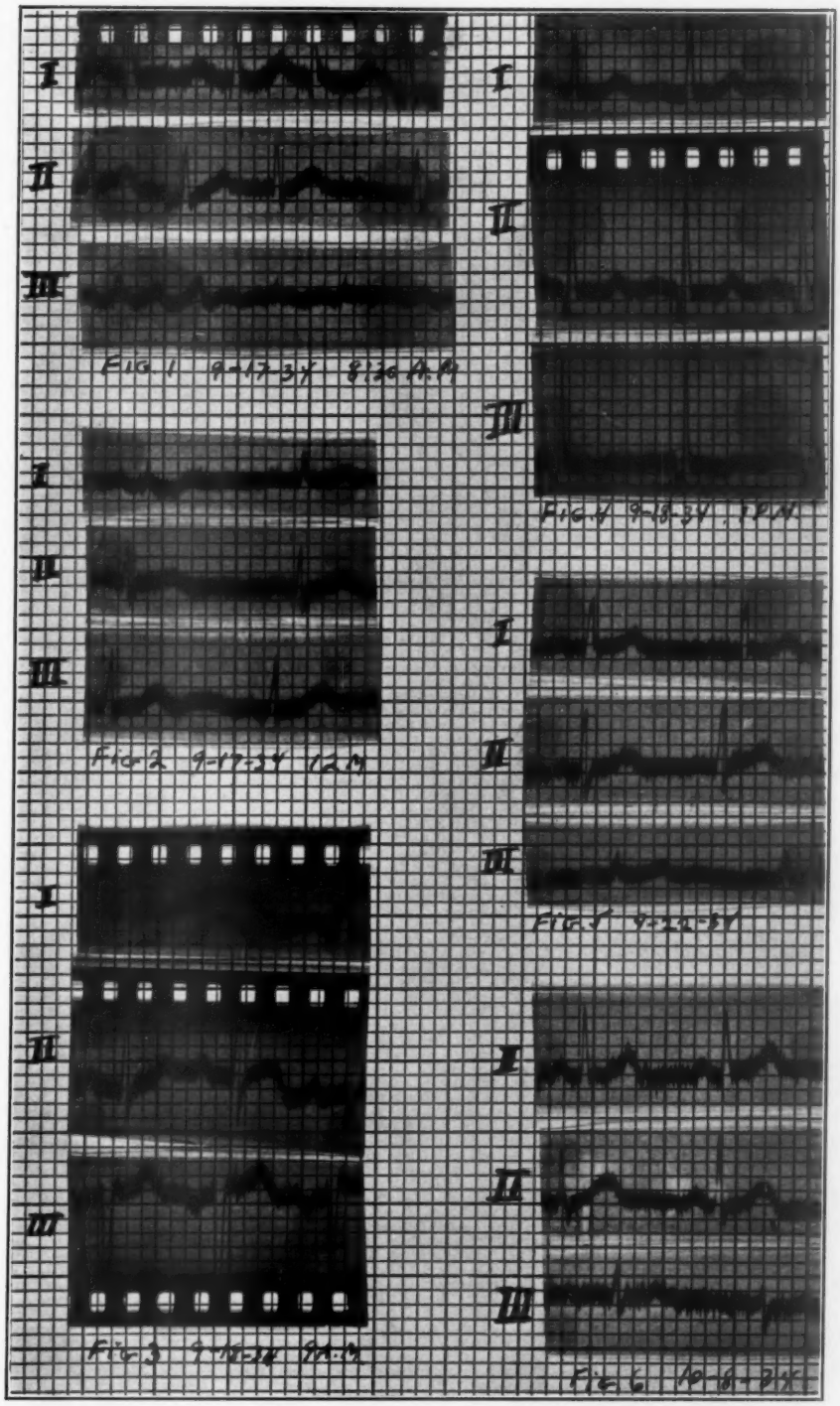
†We are indebted to Dr. Miles for the privilege of reporting this case.



Figs. 1-6.

in the same lead. At 1:00 P.M. the same day the P-R conduction time was reduced to 0.16 sec., and the P-wave in Lead III became almost isoelectric with tendency toward the diphasic (Fig. 4). The left axis deviation had entirely disappeared. The previously negative T-wave in Lead I had become definitely positive while the positive T-wave in Lead III became negative. The S-wave which was present in Lead II before had disappeared, and a large Q-wave appeared in that lead as well as in Lead III. The QRS voltage was definitely increased in Lead II.

Four days later, on September 22, the tracing was essentially normal except for the QRS voltage, which was slightly lower than the accepted minimal normal (Fig. 5). There was a tendency toward left axis deviation, and the QRS and T complexes were similar to the first tracing. On October 6, sixteen days later, the tracing was similar to the one of September 22, with the QRS voltage reaching normal (Fig. 6).

COMMENT

The tracings were all taken with the patient in the same recumbent posture; shifting of the axis, as well as the changes in the complexes, cannot be attributed to any change in position of the patient. In the absence of any demonstrable clinical evidence of cardiac disease, the progressive, rapid electrocardiographic changes could be explained on the theory of disturbance in the electrical conductivity of the heart induced by the extrinsic electric current. Judging from the changes it is quite conceivable that the temporary unconsciousness of the patient for two minutes immediately after receiving the electric shock might have been due to temporary ventricular fibrillation which soon subsided.

Department of Reviews and Abstracts

Selected Abstracts

Cossio, P., and Menendez, E. Braun: Physiological Reduplication of the Heart Sounds. Rev. argent. de cardiol. 2: 149, 1935.

Even under normal conditions the physiological auricular heart sound, which is not audible as a rule, may be exaggerated and heard. This is the most frequent cause of the so-called "reduplication of the first sound."

When the third heart sound is perceptible in the second or third interspace, on account of its vicinity to the second sound, it may be taken as a reduplication of the latter.

By direct auscultation, the frequency of occurrence and the characteristics of the physiological reduplication of the heart sounds were determined in 100 individuals under perfect circulatory conditions. The group was formed of 25 children (5 to 10 years old), 25 adolescents (18 to 22 years old), 25 adults (35 to 55 years old), and 25 elderly people (70 to 110 years old).

Reduplication of the first heart sound was found in 15 out of the 100 persons, 2 children, 5 adolescents, 1 adult and 7 elders. Reduplication of the second heart sound was found in 20 (12 children, 7 adolescents, and 1 adult).

When the reduplication of the first heart sound occurred, both components occurred one immediately after the other, without intervening silence. The first component was always deeper and less intense than the second one.

In the cases of reduplication of the second sound there generally occurred a short silence, the first component being louder, snappier and higher than the second one.

The graphic registration of the heart sounds together with the electrocardiogram (in reduplicated first sound) or with the central venous pulse (in reduplicated second sound), of 22 patients with either first or second reduplicated heart sounds showed the following findings: Reduplication of the first sound was present in eight records; in three of them the second sound was also reduplicated. Reduplication of the second sound was found in fourteen cases besides the three already mentioned.

The records showed that in 62.5 per cent of the cases the first sound reduplication was due to the occurrence of an auricular sound. Asynchronous valvular play was probably the cause of the remaining cases. In both cases there was a true reduplication.

The records showed that in 69 per cent of the cases the reduplication of the second sound was only apparent, there really occurring a third heart sound more distinctly heard on the second or third left intercostal space, especially at the end of inspiration. In 23 per cent of the cases reduplication was considered as due to sigmoid asynchronism. In the remaining 17 per cent both a reduplication by sigmoid asynchronism and a third heart sound coexisted.

The suggestion is advanced that the third heart sound, better heard on the second interspace and accentuated during the final moments of inspiration, is a third sound originated in the right ventricle.

AUTHOR.

Roberts, George H., Crawford, J. H., and Abramson, David I.: Experimental Bundle Branch Block in the Monkey. J. Clin. Investigation 14: 867, 1935.

Following division of the left main branch of the His bundle in the rhesus monkey, the chief initial deflection of the electrocardiogram is upright in Lead I and downward in Lead III.

Division of the right branch results in initial deflections downwardly directed in Lead I and either upward or downward in Lead III.

Stimulation of the ventricle contralateral to the lesion produced complexes, the deflections of which corresponded in direction to those of the bundle-branch block.

The recorded data are further evidence in support of the new terminology of bundle-branch block localization.

AUTHOR.

Youmans, J. B., Akeroyd, J. H., Jr., and Frank, Helen: Changes in the Blood and Circulation With Changes in Posture. The Effect of Exercise and Vasodilatation. J. Clin. Investigation 14: 739, 1935.

The exchange of fluid between the blood and tissues, primarily controlled by capillary and colloid osmotic pressure, is greatly influenced by a number of secondary factors, particularly by posture. The great tendency to edema in the quiet erect posture is opposed by a rising colloid osmotic pressure and by an increasing tissue pressure in the feet and legs. These forces are aided by a decrease in the volume and velocity of the circulation in the legs. With muscular activity an even greater volume of filtrate than occurs on quiet standing is prevented from accumulating by a more active lymphatic drainage. Variations in these secondary factors will influence the exchange of fluid between the blood and the tissues and, in the presence of even slight changes in the serum proteins and capillary pressure, may determine the appearance or nonappearance of edema. Due consideration must be given to the influence of these secondary factors in interpreting the effect of abnormal variations in the fundamental forces concerned, especially under conditions of changing activity such as exist in ambulatory patients. For these reasons it is inadvisable to define too strictly the critical level of the serum proteins or venous pressure in relation to the pathogenesis of certain forms of edema.

AUTHOR.

Berliner, Kurt: The Effect of Calcium Injections on the Human Heart. Am. J. M. Sc. **191:** 117, 1936.

Intravenous injection of 10 c.c. of a 20 per cent calcium gluconate solution produced changes in the electrocardiograms of twenty-six normal individuals.

These changes consisted of flattening or inversion of the T-waves in 92 per cent of the cases, flattening or inversion of the P-waves in 54 per cent, and marked bradycardia in 67 per cent.

Intravenous injection of 10 c.c. of physiological salt solution given to eighteen normal individuals had no effect whatsoever on the electrocardiograms.

This investigation, for the first time, supplies experimental proof of the effect of calcium on the normal human heart.

AUTHOR.

Levine, Harold D., and Levine, Samuel A.: An Electrocardiographic Study of Lead IV With Special Reference to the Findings in Angina Pectoris. Am. J. M. Sc. **191:** 98, 1936.

In twelve instances in which the Q-wave was absent in Lead IV either at the left sternal border or at the apex, infarction of the ventricle was found. Two cases with bundle-branch block and one of tuberculous pericarditis with absent Q_4 showed no infarction.

There were fifteen patients with small Q_4 (2 mm. or less), about half of whom had infarction and the other half did not.

Upright T-waves in Lead IV were found when no infarction was present and, in fact, where there was no significant heart disease.

In eleven cases in which the heart was normal and in one with posterior infarction, Lead IV was normal.

Evidence is presented to show that myocardial infarction is not uncommon in angina pectoris when there is no clinical evidence of a previous coronary thrombosis. Sixteen of 100 cases showed an absent Q_4 and in eleven of these the customary three leads were essentially normal.

Apart from the changes in Lead IV which occur during the acute phases of coronary thrombosis, the authors believe that the absence of Q_4 is very helpful in the diagnosis of a previous myocardial infarction, except when bundle-branch block is present.

Lead IV is indispensable in the proper diagnosis of certain cases of heart muscle disease.

AUTHOR.

Faulkner, James M.: The Electrocardiographic Diagnosis of Acute Cardiac Infarction With Special Reference to the Value of Precordial Leads. New England J. Med. **213:** 1215, 1936.

In a series of electrocardiograms including precordial leads on 250 patients, a diagnosis of fresh cardiac infarction was made fifty-one times. In eight of these the diagnostic feature was present at some time only in the chest lead, and in three it was never present in the standard leads. A comparison between the electrocardiographic and the autopsy findings was made in thirty-three cases. Out of thirteen cases with acute infarction the electrocardiographic diagnosis was positive in eleven. Localization of the infarct was not reliable by the method used. Of the twenty patients who did not show infarction, four had a questionable electrocardiographic diagnosis, and in the remainder it was negative.

The findings here recorded support the following conclusions:

1. During the first two weeks after the development of cardiac infarction, the electrocardiogram is a highly accurate method of determining the diagnosis.

2. The precordial lead offers additional information of definite value in the diagnosis of fresh cardiac infarction.

AUTHOR.

Horn, Henry, and Saphir, Otto: The Involvement of the Myocardium in Tuberculosis. Am. Rev. Tuberc. **32:** 492, 1935.

The literature of instances of tuberculosis of the myocardium is reviewed. Three main types can be differentiated, namely, the nodular, the miliary, and the diffuse infiltrative types. The last should be accepted only if either the histological changes undoubtedly are characteristic of tuberculosis or if the tubercle bacillus can be demonstrated either by guinea pig inoculation or by staining methods. Otherwise, this form of tuberculosis cannot be differentiated from the so-called specific productive myocarditis (Saltykow, Gierke). For similar reasons it is difficult to attribute to a tuberculous origin, fibrous myocardial lesions which may be present in the hearts of subjects dying of tuberculosis. Hence, the term chronic interstitial tuberculous myocarditis should be discarded.

Three instances of miliary tuberculosis of the myocardium are reported, one of which also revealed a conglomerate tubercle. These three instances occurred in children. The literature also discloses that the greater percentage of miliary tubercles in the myocardium occurred in children. This may indicate that the finding of

miliary tubercles in the hearts of young subjects dying of miliary tuberculosis is attended with less difficulty because of the relatively larger areas examined histologically.

AUTHOR.

Stevenson, Ralph R. and Turner, William J.: Rupture of a Papillary Muscle in the Heart as a Cause of Sudden Death, Bull. Johns Hopkins Hosp. 57: 235, 1935.

Nineteen cases of rupture of a papillary muscle in the heart have been reported in the literature. These cases have been summarized, and one more has been described. The usual cause is coronary occlusion and infarction of the myocardium. Rupture of the left anterior papillary muscle is usually preceded by occlusion of either the anterior descending branch of the left coronary artery or of the first descending branch of the circumflex portion of the left coronary. Rupture of the left posterior papillary muscle is associated with occlusion of both the right artery and the circumflex branch of the left coronary artery.

Sudden death occurred in half of the cases which have been reported. The condition might be suggested clinically by the sudden onset of a loud whistling to-and-fro murmur occurring in association with the signs and symptoms of coronary occlusion and cardiac infarction.

AUTHOR.

Sampson, John J.: The Prognosis of Bundle-Branch Block and Other Intraventricular Conduction System Lesions. Am. J. M. Sc. 191: 88, 1936.

One hundred and fifty-seven cases of classical bundle-branch block and 112 cases of heterogeneous atypical intraventricular conduction defect (as demonstrated by electrocardiograms) have been reviewed in an effort to estimate the prognosis of these groups.

Certain prognostic findings seem to characterize these groups and their elements. Especially to be noted is the high fatality occurring in cases of bundle-branch block during the first year after the discovery of the lesion or in the first 20 per cent of the life expectancy and the remarkable diminution of the case fatality rate in the groups which survive these periods.

AUTHOR.

Hamman, Louis, and Rienhoff, William F.: Subacute Streptococcus Viridans Septicemia, Bull. Johns Hopkins Hosp. 57: 219, 1935.

A man, thirty-five years of age, was ill with *Streptococcus viridans* septicemia without evidence of a valvular defect in the heart. There was a diagnosis of an arterial venous aneurysm between the external iliac artery and vein. In the absence of evidence of heart disease, it was decided that the *Streptococcus viridans* septicemia was originating from the infected focus in the walls of the aneurysm. At operation the aneurysm was ligated and removed. Following the operation there has been a complete recovery. A description of the specimen removed at operation is included.

Dana, Harold W., and Reidy, John A.: Mitral Valve Disease. Pathological Report. Am. J. M. Sc. 191: 109, 1936.

One-half of all cases of rheumatic endocarditis of the mitral valve show no stenosis of this valve at autopsy, even in cases known to have been of many years' duration.

Pure mitral stenosis is rarely found at autopsy, it cannot be recognized with certainty even when present, and modern physiological study would seem to suggest that the clinical importance of mitral stenosis is at present too much emphasized.

Pure mitral regurgitation is not uncommon, occurring in one-fifth to one-half of all cases of rheumatic endocarditis of this valve; it can of itself cause death, and it is believed that regurgitation is entitled to a more prominent place than it now holds in the study of mitral disease.

Clinical and pathological analyses were made of 150 cases of mitral endocarditis, after a preliminary study of about 300 hearts to establish standards for comparison.

One clinical case history, with autopsy findings, is presented.

AUTHOR.

Coburn, Alvin F., and Pauli, Ruth H.: Studies on the Immune Response of the Rheumatic Subject and Its Relationship to Activity of the Rheumatic Process. J. Clin. Investigation **14**: 783, 1935.

The findings presented in earlier papers of this series led to two conclusions: First, both influenza virus and one type of hemolytic streptococcus were ineffective in initiating recrudescences in a rheumatic colony. This strain of streptococcus did not produce soluble toxin, and although present in the throat, flora was not associated with acute infection. Second, another type of hemolytic streptococcus was highly effective in initiating recrudescences in fourteen out of sixteen rheumatic members of this same colony. This strain was a strong toxin producer, was associated with acute infection of the upper respiratory tract, and was a single serological type. In addition to infection with an effective strain of hemolytic streptococcus, two other factors contributed to the development and character of this epidemic of acute rheumatism. These factors were, first, the disease pattern peculiar to each rheumatic subject, and second, the intensity of the immune response.

Next it was pointed out that most strains of hemolytic streptococcus which are effective in producing acute rheumatism form soluble toxin and streptolysin and are indistinguishable from scarlatinal strains. Most of the strains associated with throat infections which are ineffective in initiating rheumatic attacks form little or no soluble toxin. This finding, in conjunction with earlier studies, indicates a close relationship between scarlet fever, acute rheumatism and toxin-producing strains of hemolytic streptococcus.

The findings presented in the fifth paper of the present series demonstrated that neither active nor passive immunization to hemolytic streptococcus inhibited the development of the rheumatic process. The observations indicated that the development of rheumatic activity depends not only upon infection with an erythrogenic strain, but also upon the host's immune response to such infection.

Next it was pointed out that there is a close time relationship between the antistreptolysin rise and the onset of rheumatic activity. A small number of rheumatic subjects were observed to be infected with strains of hemolytic streptococcus which produced strong toxin and streptolysin and nevertheless failed to develop a significant rise in antistreptolysin titer. These individuals also failed to develop a rheumatic attack. The authors interpret this fact to mean that, in addition to infection with an effective strain, stimulation of the host sufficient to produce an antibody response is essential to initiation of rheumatic activity. It seemed that the character of the antibody response played a large part in determining the type of the rheumatic attack.

Finally, the observations made in the present paper indicate that in the patients who escaped postsplenectomy rheumatic recrudescences, the antibody-producing tissue was presumably quiescent; and that in those patients who developed acute rheumatism following splenectomy, the antibody-producing tissue was probably in a state of activity. Likewise, as was already pointed out, in the subjects who escape recrudescences following infection with hemolytic streptococcus, the antibody-pro-

ducing tissue presumably remains quiescent; and in those subjects who develop acute rheumatism following hemolytic streptococcus infection, the antibody-producing tissue is activated. These two sets of observations together show that acute rheumatism may follow either activation of the antibody-producing system by hemolytic streptococcus or operative manipulation of this system during the period in which it is producing immune bodies to hemolytic streptococcus.

It is the authors' conception that rheumatic disease is the result of the following sequence of events: (1) Infection with toxin-producing strains of hemolytic streptococcus initiates a process peculiar to rheumatic subjects. (2) In the course of this process a substance is released, presumably from the antibody-producing tissues, which either directly or indirectly alters mesodermal structures. This substance is probably not the infecting organism, and at the present time there is no evidence to suggest that it is viable. (3) The release of this toxic substance seems to take place only when there is an immune response to hemolytic streptococcus.

In conclusion, the collected evidence indicates that activity of the rheumatic process depends not only upon effectiveness of the infecting strain of hemolytic streptococcus but also upon the intensity of the immune response of the rheumatic subject to this bacterial agent.

AUTHOR.

Blackford, L. Minor: Syphilitic Aortic Insufficiency. J. M. A. Georgia 24: 341, 1935.

Seven cases of syphilitic aortic insufficiency representing about 5 per cent of the total series studied led to the following conclusions:

Syphilis of the aorta can be prevented by the thorough treatment of every case of syphilis in its early stages. In spite of the two cases reported in which it was apparently beneficial, the use of neoarsphenamine in the usual dosage in the treatment of syphilis of the aorta is fraught with grave danger.

An occasional patient with syphilitic aortic insufficiency will live comfortably for a number of years without any treatment. Careful regulation of the mode of living, treatment with bismuth, potassium iodide, and digitalis will often serve to make the patient with syphilitic aortic insufficiency more comfortable, and probably permit him to live longer.

AUTHOR.

Taussig, Helen B.: Essential Hypertension in Boy Two Years of Age, Bull. Johns Hopkins Hosp. 57: 183, 1935.

The case is that of a two-year-old colored boy with hypertension, cardiac enlargement, and progressive cardiac failure. The hypertension was present throughout the period of observation, and probably had already existed for several months. The autopsy yielded little, if anything, of a positive nature to explain the hypertension. The lesions in the kidneys appeared to be too slight, too widely scattered, and of too recent origin to form the basis for the known duration of the hypertension.

Menendez, E. Braun, and Orias, O.: Duration of Phases of the Cardiac Cycle in Hypertension. Rev. argent. de cardiol. 2: 186, 1935.

The duration of the cardiac phases was determined from the venous pulse recorded in twenty-six patients with arterial hypertension and in thirty normal persons.

The duration of the phases of the cardiac cycle in patients with arterial hypertension showed significant differences as compared with that of the normal individuals.

Total systole is prolonged, especially at the expense of the ejection phase (+ 0.03 ± 0.005 sec.), whereas the isometric contraction is reduced (0.04 ± 0.002 instead of 0.05 ± instead of 0.10 ± 0.002 sec.). The difference (0.04 ± 0.005 sec.) is significant.

AUTHOR.

Cranch, A. G.: Hypertension With Relation to Capacity for Work. Ohio State M. J. 31: 676, 1935.

Hypertension is probably more common in industry than is generally supposed. Care must be taken to avoid error in detection of cases. Itself only a symptom, associated conditions must receive the greatest consideration. From the point of view of capacity for work, myocardial and arteriosclerotic changes are most important. Standards based primarily on blood pressure determinations are not satisfactory. Successful placement of hypertension cases is possible only through continuing supervision.

It is believed that the findings with regard to diastolic pressure are commonly of more significance than those of systolic pressure in estimating the capacity for work. Particular attention should be given to cases which show steadily rising pressures on succeeding examinations, and those cases which show evidence of myocardial deficiency or marked arteriosclerotic changes.

AUTHOR.

Wartman, Wm. B.: A Study of the Venous Blood Pressure in Some Common Diseases, Am. J. M. Sc. **190:** 464, 1935.

1. The results of 366 determinations of the venous blood pressure in 215 patients suffering from various diseases have been presented.

2. In a control series of thirty-one patients who showed no evidences of circulatory disease, the average venous pressure was 83 mm. H_2O, and the difference of the two readings with the standard deviation of the difference was 16 mm. H_2O = 11 mm. H_2O.

3. An increase in venous pressure was observed only in patients suffering from cardiac failure with congestion or mediastinal obstruction.

4. Serial determinations of the venous pressure were of value in following the course of cardiac cases; a shift toward the normal indicated a favorable prognosis, but a progressive increase in pressure was an unfavorable sign.

5. The arterial and venous blood pressures appear to be independent, in the sense that a change in one does not necessarily affect the other.

6. The presence of pulmonary tuberculosis, bronchial asthma, or lobar pneumonia did not influence the venous pressure of the cases studied.

7. When an increase in venous pressure occurred in any disease, it usually indicated beginning circulatory failure.

8. Of the patients with a venous pressure over 250 mm. H_2O, 69 per cent died within three months, whereas only 8 per cent of those with a pressure below this critical level succumbed.

AUTHOR.

Head, Jerome R.: Effect of High Intrapleural Pressure on Blood Pressure. Arch. Int. Med. 56: 904, 1935.

It can be said that high pressure in the pleural cavity acts directly on both the pulmonary and the systemic circulation, on the former by collapsing the lung and on the latter by compressing the great veins.

Collapse of the lung causes: (1) a decrease in the flow of blood throughout the collapsed lung, (2) a rise in pressure in the pulmonary circulation, (3) an increased strain on the right heart, and (4) a reduction in the vital capacity.

Compression of the great veins causes: (1) a rise in the venous pressure, (2) an insufficiency in the return of venous blood, and (3) a decreased output of the heart.

Up to relatively extreme degrees of pressure these hindrances are compensated for by an increase in tone of the vasoconstrictor center. The first sign of the strain on this compensatory mechanism is an exaggeration of the Traube-Hering waves, a tendency for the peripheral resistance to give way during inspiration. A time comes when the center can no longer fully compensate, and the mean blood pressure falls below the critical level.

AUTHOR.

Marinescu, G., Bruck, H. A., and Vasilescu, N.: Capillary Circulation in Organic Hemiplegia. Ztschr. f. Klin. Med. **127**: 578, 1934.

In the affected extremities of organic hemiplegia the following vasomotor and humoral changes were observed: (1) dilated capillaries in which there was a slower blood flow; (2) slower refilling of the capillaries after compression (20-21 seconds) than in the normal subjects (15-17 seconds); (3) diminished absorption capacity of the capillaries and veins after compression; (4) reduction and retardation of active dilation of blood vessels after compression; (5) increased alkalinity of the blood (5.7-11 per cent); (6) lowering of the viscosity of the blood; (7) presence of edema and acroasphyxia due to change of tonus in the peripheral blood vessels; and (8) abnormal dilation of the vessels in the affected extremity following the injection of calcium.

J. K.

Urban, H.: Arteriography of the Brain. Wien klin. Wchnschr. **48**: 924, 1935.

Arteriography of the brain is valuable from the diagnostic standpoint when the neurological findings do not indicate clearly the type and location of the brain lesion. No reactions were noted as a result of the use of the thorotrast for arteriography following the technic of Moniz. Ten cubic centimeters of thorotrast are injected into the internal carotid artery after it is exposed by incision. Injection must be made quickly, and the picture must be made immediately thereafter as the thorotrast disappears from the brain after three seconds.

J. K.

Herrmann, L. G.: Nonoperative Treatment of Inadequate Peripheral Distribution of Blood: Passive Vascular Exercises and Local Hyperthermia. J. A. M. A. **105**: 1256, 1935.

The results of passive vascular exercises (pavaex therapy) in dealing with suddenly or gradually occluded arteries of the extremities have been evaluated by Herrmann and found satisfactory. The author draws his conclusions from some 50,000 hours of pavaex therapy given to several hundred patients in the first thirty-three months of its use in his clinic.

One of the most remarkable results obtained has been in preventing the serious sequelae of extensive thermal trauma to the extremities in all cases treated by this method.

Herrmann emphasizes the object of the treatment, to develop adequate collateral circulation around the obstructed artery or arteries; and likewise the fact that clinical judgment must be used in selecting cases. Sudden obliteration of major arterial pathways offers the most opportunity for striking clinical benefit.

In thromboangiitis obliterans, Herrmann believes the method offers only temporary relief due to the extensive obliteration of arteriolar and small arterial beds which characterizes the disease.

For the past year preheated dry air at an average temperature of 104° F. (local hyperthermia) has been combined with the pavaex therapy with encouraging effect. This is thought to be due in part to the release of concomitant vasospasm, in part to increase of the metabolism of the tissues as the collateral blood supply is simultaneously augmented.

L. H. H.

Reimann, F., and Breuer, A.: Venesection Therapy of Polycythemia Vera. Ztschr. f. klin. Med. **128**: 238, 1935.

Systematic venesection was used in seven cases of polycythemia vera. Three hundred to five hundred cubic centimeters of blood were withdrawn twice weekly until the hemoglobin in the blood was lowered to 80 or 90 per cent. The repeated bleedings reduced the number of circulating erythrocytes and relieved the patients of their subjective complaints. Venesection is not only symptomatic therapy, but at the same time it attacks the principal mechanism of blood regeneration by reducing reserve material, principally iron, which is necessary for the production of red cells and hemoglobin. In several cases total remission of polycythemia was observed, and one patient remained without complaints for three years. The result of repeated venesection in polycythemia proved to be equal to, if not superior to, the usual therapy with x-rays and phenylhydrazine.

J. K.

Johnson, Carl A.: Studies of Peripheral Vascular Phenomena: IV. The Effect of Artificial Fever on the Pulse Volume Changes of the Finger, Am. J. M. Sc. **190**: 485, 1935.

The effects of artificial fever upon the peripheral circulation have been presented and may be briefly summarized as follows:

1. There was a marked increase in the pulse-volume changes of the fingers with all types of artificial fever used, except foreign protein which gave a primary decrease associated with the chill, but followed by an increased circulation.

2. The vasodilatation of foreign protein fever is probably of central origin while the vasodilatation with artificial fever induced by external heat and preventing heat loss is chiefly of peripheral origin.

3. The maximum increased circulation from artificial fever occurred in general at temperatures between 103° and 104° F. while the maximum temperature used was 104.5° F. This suggests that there is an optimum temperature at which peripheral circulation reaches a maximum.

4. Artificial fever from external heat and prevention of heat loss is dangerous and should not be used unless adequate facilities are available and should not be left in the hands of a technician.

Atchley, Dana W.: The Rôle of Peripheral Circulatory Failure in Clinical Medicine, New England J. Med. **213**: 861, 1935.

In this address before the New England Heart Association, the author describes the picture of peripheral circulatory failure from varying causes, especially those conditions without cardiac failure. He believes that dehydration and salt depletion account for the picture of peripheral circulatory failure and for the classical syndrome of shock. He believes that an estimation of venous pressure is of importance

in differentiating this type of shock from cardiac failure. He describes briefly the treatment for the condition, emphasizing the need for the restitution of salt, together with the introductions of serum protein by means of transfusion of blood or other colloidal substances, such as acacia.

AUTHOR.

Veal, J. Ross, and McFetridge, Elizabeth M.: Primary Thrombosis of the Axillary Vein. An Anatomic and Roentgenologic Study of Certain Etiologic Factors and a Consideration of Venography as a Diagnostic Measure. Arch. Surg. 31: 271, 1935.

Two cases of primary thrombosis of the axillary vein are presented. Roentgenological and anatomical studies prove clearly that constriction of the vein occurs, not as previously believed over the first rib beneath the subclavius muscle, but below the head of the humerus and against the subcapsularis muscle. The stretching of the vein takes place only within the part of the vein just proximal to the point of constriction below the head of the humerus. The emptying time of the vein is actually more rapid in the position of hyperabduction and external rotation than when the arm is held at an angle of 45 degrees to the body. The increase in the venous pressure is brought about not by change of position itself but only when additional factors of strain are introduced. However, the etiology of primary axillary vein thrombosis has not been determined, although the reasonable assumption is that the constant underlying factor is some individual anatomic variation. Venography allows clear deliniation of the obstructed area and of the pathways through which blood flows toward the heart.

E. A.

Anrep, G. V., and Von Soalfeld, E.: The Blood Flow Through the Skeletal Muscle in Relation to Its Contraction. J. Physiol. 85: 375, 1935.

Muscular contraction is accompanied by compression of intramuscular blood vessels. This compression and subsequent vasodilatation depend on the strength of the muscular contraction. Potent vasodilating substances appear in the venous blood emerging from a contracting muscle. They are produced and released during muscular contraction and are stable in the blood for half an hour at least.

E. A.

Nicole, R.: Arteriospasm in Acute Thrombosis of the Veins. Schweiz. med. Wchnschr. 65: 676, 1935.

The presence of a spastic occlusion of the femoral artery resulting from acute thrombosis of the femoral vein is described. The femoral artery was contracted for several hours. The skin showed signs of ischemia. Such cases are often mistaken for arterial embolism and are operated on without success. The arterial spasm is perhaps due to a regulating mechanism for averting increased blood supply which could not be carried away by the closed vein. Therapy consists of rest, elevation, and heat.

J. K.

Clark, Eliot, R., and Clark, Eleanor Lintow: Observations on Changes in Blood Vascular Endothelium in the Living Animal. Am. J. Anat. 57: 385, 1935.

Observations on blood vessels in living amphibian larvae and in transparent chambers inserted in rabbits' ears indicate that endothelium undergoes a series of changes.

Phase 1.—The lining is smooth; tonicity, elasticity, and contractility (amphibians only) are present.

Phase 2.—No impairment of tonicity, elasticity, and contractility. The consistency of the endothelium changes slightly and leucocytes may stick to the wall momentarily.

Phase 3.—Endothelium becomes sticky and leucocytes cling to the walls. Tonicity and elasticity are not impaired.

Phase 4.—Consistency of endothelium becomes softer; leucocytes push through to outside tissue.

Phase 5.—Endothelium is subjected to mechanical or chemicay injury. Tonicity and elasticity are lost, and leucocytes lose their mobility.

Phase 6.—Serious injury to the endothelium which causes it to separate into solid, rounded, hyalin globules which are injested by macrophages. Endothelium damaged this badly does not recover.

The rapidity with which changes in endothelial consistency may take place and the relatively minute stimuli necessary to elicit certain of these changes, together with their reversibility, are of unquestionable physiological importance and should be taken into account in any comprehensive consideration of the morphology and physiology of blood vascular endothelium.

E. A.

Montgomery, A. H., and Ireland, J.: Traumatic Segmentary Arterial Spasm. J. A. M. A. 105: 1741, 1935.

After experiencing two instances of spasmodic occlusion of the normal brachial artery in the vicinity of a fracture, proved by operative exposure, the authors searched the literature for reports of similar alarming episodes. They found the condition reported infrequently, and almost exclusively by continental European surgeons.

The reports, as in their own cases, dealt only with large arteries of the extremities, which remained bloodless cords for minutes to hours for a varying distance from the site of trauma. Gunshot wounds and fractures were blamed for thirty-six of the forty-four cases investigated.

The spasm generally relaxed within twenty-four hours. In those cases in which the occluded portion was excised, thrombosis was never found. The condition is considered due to a sympathetic nerve imbalance causing the spasmodic constriction, or possibly, in the light of recent work, to a chemical factor released by the trauma.

The authors advise conservative measures of treatment at first, and if the circulation does not return after reduction of the fracture or care of the wound, then exposure of the artery and application of continuous warm moist dressings.

L. H. H.

Ross, J. P.: The Results of Sympathectomy. An Analysis of the Cases Reported by Fellows of the Association of Surgeons. Brit. J. Surg. 23: 433, 1935.

About 250 records of various types of operation on the sympathetic nervous system were submitted, one-fourth of which were adequate to show late results of sympathectomy. Ganglionectomy was invariably successful in sixty-one cases of Raynaud's disease unless complicated by scleroderma.

In thromboangiitis obliterans, with intermittent claudication only, the effect of ganglionectomy was slight or nil in twenty-nine instances reported. Rest pain was relieved and gangrene arrested in a majority of thirty-seven cases of that disease. Clinical criteria for choice of patients did not show up clearly in the reported cases.

The results of sympathectomy applied to other pathological states including poliomyelitis-paralyzed limbs with circulatory disorders, Hirschsprung's disease, renal pain, and causalgia were more good than otherwise. Even periarterial sympathectomy in twenty cases of gangrene brought relief of pain or unexpected arrest of several of the gangrenous processes.

Indeed, the results of the analysis bespeak a care in selection of cases for sympathetic system surgery and a technical efficiency which are remarkable. One can only hope that later reports on follow-up and a more extensive series of cases will turn out as well.

L. H. H.

Burge, W. E., Orth, O. S., Neild, H. W., Ash, J., and Krouse, R.: Mechanism of Pathological Calcification. Arch. Pathol. **20:** 690, 1935.

The authors recall briefly some of the recent theories of calcification in the soft tissues of the body. The suggestion is then made from their experimental results that the electronegativity of active, injured or dying tissue is due to negatively charged phosphate ions at the site. A demarcation current set up by the difference in potential between cut or injured surface of tissue and an uninjured or inactive portion was abolished by applying positively charged calcium or barium ions to the injured area. This is considered due to the combination of the positively charged ions with the negatively charged phosphate ions to form insoluble and nonionized barium or calcium phosphate.

The method was applied to the injured intima of arteries, and the same results occuring, the authors atribute pathological calcification of arteries to the insoluble calcium phosphate thus precipitated at the point of injury of the wall.

L. H. H.

Perlow, S., and Vehe, K. L.: Variations in the Gross Anatomy of the Stellate and Lumbar Sympathetic Ganglia. Am. J. Surg. **30:** 454, 1935.

The authors, stimulated by the recent growth of surgical procedures involving the sympathetic nerves and ganglia, dissected out the stellate and lumbar ganglia and immediate connections in twenty-four cadavers. They present, with the aid of drawings, the variations in size, position and connections of the ganglia which they observed.

L. H. H.

Rusznyak, S., Karady, I., and Ezaba, D.: Experiments to Prevent Postoperative Shock Syndromes. Deutsche med. Wchnschr. **61:** 1111, 1935.

Patients who are predisposed to postoperative shock show a characteristic blood pressure reaction after injection of 0.005 mg. histamine intravenously. The systolic blood pressure is diminished for a short time following the injection of histamine and then increases greatly. Subcutaneous injections of 0.5 to 1 mg. of histamine for several days in succession can change this type of reaction to one in which there is no increase in the blood pressure. It would seem that repeated injections of histamine before operation might prevent circulatory collapse which may follow operation.

J. K.

Voelker, Heinrich: Examination of the Circulation Time in the Lung. Determination of the Shortest Lung Circulation Time. Ztschr. f. d. ges. exper. Med. **96:** 482, 1935.

In experimenting on the lungs of cats, to determine the circulation time, the modified Stewart method was used—injection of glucose into the jugular vein. The time which is necessary for the glucose to reach the carotid artery is the circulation time in the lung. The difference in the time when glucose can be

identified in blood from the femoral and carotid arteries is the circulation time in the aorta. The average circulation time of the lungs was 3.2 seconds; the rate of circulation in the aorta was 12 meters per second. Chloroform used as an anesthetic instead of ether increased the circulation time in the lung by 2 seconds and slowed down the circulation in the aorta to 4 meters per minute. Avertin administered by rectum did not change the circulation time of the lung. Inhalation of CO_2 slightly lowered the circulation time of the lung and increased the circulation in the aorta. Bloodletting changed the lung circulation only very slightly. After eventration there was a slight decrease in the aorta circulation time, but the lung circulation stayed nearly unchanged. This shows that the lung circulation is kept nearly constant by the organism in spite of great changes in the general circulation.

J. K.

McGovern, T., McDevitt, Ellen, and Wright, Irving S.: Theobromine Sodium Salicylate as a Vasodilator. J. Clin. Investigation **15**: 11, 1936.

Twenty patients suffering from one or more of various peripheral vascular diseases were studied to determine the claims made for theobromine and its salts as efficient vasodilators, suitable for use in the treatment of peripheral vascular disease. Patients were studied under standard controlled environmental conditions, and the effect of the drug on skin temperature of various parts of the body, pulse, respiration, and blood pressure changes was noted.

It is concluded from this study that theobromine sodium salicylate in the dosage and by the methods of administration used is too unreliable and feeble a vasodilator to be of value in the treatment of peripheral vascular disease.

AUTHOR.

Resnik, Harry, Jr., Friedman, Ben, and Harrison, T. R.: Effect of Certain Therapeutic Measures on the Cardiac Output of Patients With Congestive Heart Failure. Arch. Int. Med. **56**: 891, 1935.

The cardiac output per minute of persons with congestive heart failure tends to be decreased by rest, venesection, morphine, thyroidectomy, and abdominal paracentesis. In proportion to the metabolic needs the output may or may not be diminished by these procedures.

In patients with auricular fibrillation the restoration of the normal rhythm with quinidine has been associated with an increase in the cardiac output.

Resection of the pericardium of a patient with obliterative pericarditis was followed by an increase in the cardiac output.

The mechanism of improvement produced by the various therapeutic measures has been discussed. It is concluded that pericardial resection produces improvement in patients with concretio cordis by allowing the heart to do more work. On the other hand, therapeutic benefit in heart failure of the ordinary type is believed to be dependent on one fundamental factor: rest of the heart as a result of diminished expenditure of energy. Such an effect may be brought about either (a) by procedures which diminish the work done by the heart or (b) by measures which increase its mechanical efficiency so that less energy is wasted.

AUTHOR.

Carr, James G., and Mayer, Jacob D.: Clinical Experience With a Derivative of Squill, Arch. Int. Med. **56**: 700, 1935.

Scillonin, a derivative of squill, will produce the usual effects of digitalis in the treatment of cardiac decompensation. Essentially the same therapeutic and toxic results are obtained as occur with the use of digitalis.

Cardiac irregularities are likely to be the first signs of dangerous intoxication. Nausea does occur and may precede the appearance of cardiac irregularities. The

nausea of scillonin intoxication is significant in that it appears to signify a more advanced grade of intoxication than that associated with the nausea of digitalis. Nausea and cardiac irregularities occurring in the course of treatment with scillonin are symptoms which call for the immediate discontinuance of administration of the drug.

Slowing of the cardiac rate to 60 or below is frequent with the successful use of scillonin. The onset of a rate as low as 60 is significant of the full therapeutic dose and calls for discontinuance of scillonin medication temporarily.

A dose of from 8 to 12 mg. of scillonin of standard potency as now provided, depending on the weight of the patient, may be given within four days to patients who are known to have taken no drug of the digitalis group within two weeks. If a prior course of scillonin or of some other drug of the digitalis group has been used with full therapeutic effect, the maximum dosage of scillonin should not be repeated within a month. Under these circumstances small doses may be given daily until the effect appears. The maintenance dose of scillonin is approximately 0.5 mg. per day, but it must be adapted to the needs and response of the individual patient. In a few cases in private practice the patient has been kept on a small daily ration for three years or more. For small patients the daily maintenance dose is as low as 0.33 mg.

Scillonin therapy is of advantage to certain persons who take digitalis with difficulty because of gastric distress early in the course of medication. Scillonin may be recommended for these patients. It is not a substitute for digitalis in the presence of frank digitalis intoxication. When digitalis has been given recently, only small doses of scillonin are permissible. The desired effect may be achieved by daily doses somewhat larger than the maintenance dose.

Scillonin retains its potency over a long period. A supply known to be about seventeen months old proved as effective at the end of that time as the lots recently assayed.

AUTHOR.

Dieuaide, F. R., Tung, C. L., and Bien, C. W.: A Study of the Standardization of Digitalis. I. A Method for Clinical Standardization. J. Clin. Investigation 14: 725, 1935.

Past efforts to standardize digitalis by clinical study are briefly reviewed.

An attempt was made to ascertain the feasibility of separating by clinical assay different strengths of the same tincture of digitalis. In the conditions of the experiments, among the phenomena observed (which included symptoms, weight, blood pressure, cardiac rate, and various aspects of the electrocardiogram), only one seemed clearly helpful. The effect, under standard conditions, of three such samples on the Q-T interval of the electrocardiogram, stated in relation to the cardiac cycle length, made it possible to distinguish potencies related as 75: 100: 125. Aged and fresh samples of the same tincture were similarly tested.

The conditions for satisfactory clinical assay of digitalis are discussed, and a standard set outlined.

AUTHOR.

Van Dyke, H. B., and Li, R. C.: A Study of the Standardization of Digitalis. II. The Relationship Between Laboratory Methods of Assay and Potency as Determined by Experimental Cumulative Poisoning and Clinical Standardization. J. Clin. Investigation 14: 733, 1935.

Two samples of leaf of *Digitalis purpurea* were found to be equally potent in mammals (cats and dogs) but to differ significantly in potency as measured by assay in frogs. They were also compared by means of cumulation experiments in dogs and by a satisfactory method of clinical assay.

The cumulation experiments in dogs (Table III) and the clinical assays (Tables IV and V) were in agreement with the assays in mammals (Table II).

AUTHOR.

Fowler, W. M., Hurevitz, H. M., and Smith, Fred M.: Effect of Theophylline Ethylenediamine on Experimentally Induced Cardiac Infarction in the Dog. Arch. Int. Med. **56**: 1242, 1936.

The experiments reported here have demonstrated that theophylline ethylenediamine promotes the development of the collateral circulation in experimentally induced cardiac infarction in the dog. The results justify the use of this preparation in the treatment of disease of the coronary arteries and acute coronary occlusion.

AUTHOR.

Dameshek, William, and Colmes, Abraham: The Effect of Drugs in the Production of Agranulocytosis, With Particular Reference to Amidopyrine Hypersensitivity. J. Clin. Investigation **15**: 85, 1936.

In twelve cases of agranulocytosis, although many etiological factors seemed operative, the only constant one was that of a drug, usually amidopyrine, administered either alone or in combination. Of eight patients who recovered, four were selected for special study of possible hypersensitivity to drugs.

One patient reacted strikingly (within 90 minutes) to the oral administration of 0.6 gm. (10 grains) of amidopyrine with the resultant clinical and hematological manifestations of agranulocytosis. Two other patients developed moderate leucopenic and clinical reactions; the fourth patient, given 0.3 gm. (5 grains) of the drug, developed no symptoms. The skin reactions to various scratch tests, patch tests, passive transfer tests, and intradermal tests with the drug alone were essentially negative. However, intradermal tests with a mixture of the drug and blood serum were strongly positive in all three cases tried.

Two of three patients, shortly after the intradermal administration of amidopyrine solutions for skin testing, developed all of the clinical and hematological features of agranulocytosis. The total quantity of amidopyrine used in these tests did not exceed 10 mg. (⅙ grain).

Numerous reports demonstrate that the use of drugs, particularly of amidopyrine both alone and in combination, is an important cause of agranulocytosis. The widspread use of these drugs and the relatively few cases of the disease suggest an idiosyncrasy or hypersensitivity on the part of certain individuals.

The experimental observations present conclusive evidence of extreme hypersensitivity on the part of certain individuals to amidopyrine. The production of agranulocytosis following the intradermal introduction of only a few milligrams of the drug tends to disprove the theory that the drug must be oxidized in the gastrointestinal tract before it can become toxic.

The negative intradermal tests with an aqueous solution of amidopyrine as contrasted with the strongly positive tests with a "serumized" solution suggest a possible drug-protein linkage as the basis of the "allergic" or hypersensitive reaction.

The fundamental mechanism by which the bone marrow becomes affected and agranulocytosis results has not yet been demonstrated. These observations together with others suggest that certain drugs may cause suppression, "maturation arrest," of granulocyte production. In an individual who is hypersensitive, "allergic," to a given drug, a minute amount may initiate the disease.

AUTHOR.

Book Review

FAILURE OF THE CIRCULATION. By Tinsley Randolph Harrison. Baltimore, 1935, 396 pages, The Williams & Wilkins Company.

This book was written by one who, with several associates, has been actively engaged for over a decade in the clinical and experimental study of the mechanism of the failure of the circulation. The structure of the presentation consists in an introduction, five sections of discussion, and a summary. A selected bibliography and author and subject indexes are appended.

In the concise historical introduction, the author presents the early history of the knowledge of circulatory failure, bearing particularly on the concepts of "forward failure" and "backward failure" of the circulation (i.e., whether the early and primary derangement of the circulation depends on the inadequate blood supply to the tissues resulting from decreased cardiac output, or on the engorgement of blood behind the failing or diseased portion of the heart). After justified apologies the author introduces the terms and concepts of hypokinetic, hyperkinetic, and dyskinetic syndromes. Whether these terms as representing basic concepts are constructive or entirely justified may be debated. Of the three syndromes, the hyperkinetic and hypokinetic syndromes are discussed in a summary fashion, while the dyskinetic syndrome (congestive failure) represents the bulk of the volume. In this part the author analyzes in detail the experimental and clinical evidence for and against the forward and backward failure theories. He concludes that the forward failure theory is not acceptable, and presents evidence favoring the backward failure theory. In the succeeding chapters, the mechanism of a number of the important phenomena of the failure of the circulation is presented in a selective manner. The conclusions of some of the chapters are reached on the basis of the analysis of the literature, and of others on the basis of rich personal experience. The chapters on dyspnea and edema are particularly good. The discussions on the classification and measurements of dyspneas, the causes of dyspnea on exertion, the mechanism of orthopnea, paroxysmal dyspnea, and Cheyne-Stokes' respiration are stimulating and reveal valuable information with much originality. The numerous other manifestations of circulatory failure are treated concisely, rather in a clinical descriptive than in an analytical manner. The section on the therapeutic action of digitalis is excellent in describing the mechanism whereby digitalis produces improvement. There is in addition a short section on the failure of the coronary circulation.

The style of the book is simple and direct. There is, however, a lack of uniformity in the construction of the chapters. The book serves as an excellent demonstration of the methods and tools used in clinical sciences today. Clinical observations and descriptions are related to results of well-conceived experimental studies, though the ratio of the correlation varies widely in different chapters, depending primarily on whether or not the author has done work on the subject. In arrangement the book is a cross between a monographic presentation and a detailed textbook of specialties. It is a well-focused and excellent presentation of the subject in the light of personal experience and opinion by one who has pondered over the problems. The book is not for the use of the average physician interested in general medicine. Rather it is a reference book for those desiring to be, or considered as, experts in diseases of the heart and the circulation, and for all students who are interested in the functional approach and analysis of clinical phenomena.

S. W.